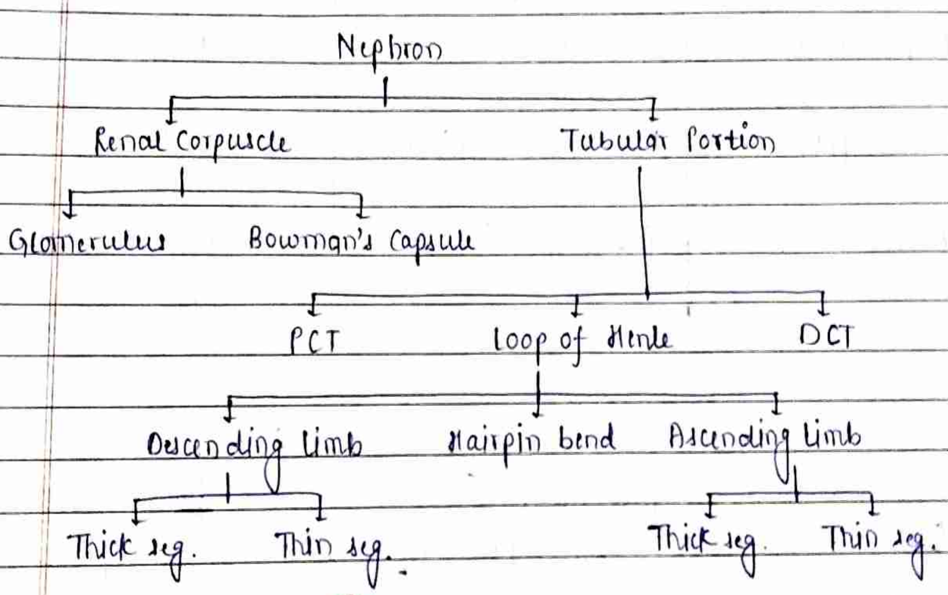
Date 26
Page

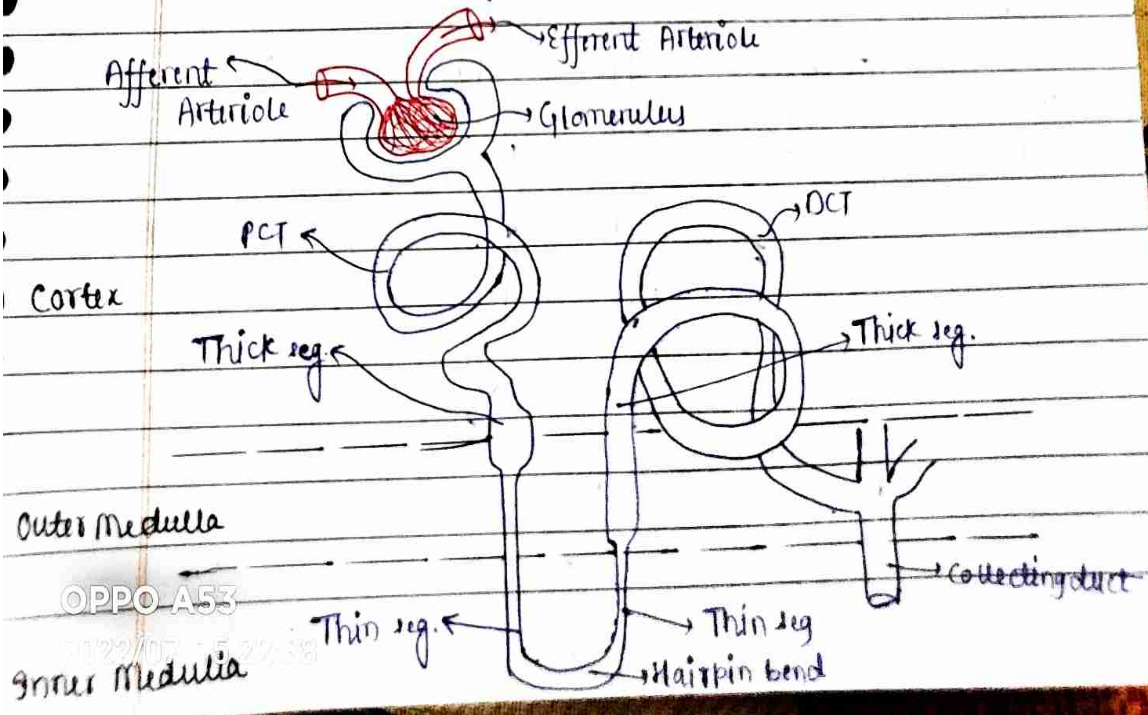
RENAL PHYSIOLOGY

① NEPHRON

→ Structural & functional unit of kidney
→ Each kidney consist about 1 million nephrons

★ Parts of Nephron


Nephron
Renal Corpuscle
Tubular Portion
Glomerulus
Bowman's Capsule
PCT
Loop of Henle
DCT
Descending limb
Hairpin bend
Ascending limb
Thick seg.
Thin seg.
Thick seg.
Thin seg.

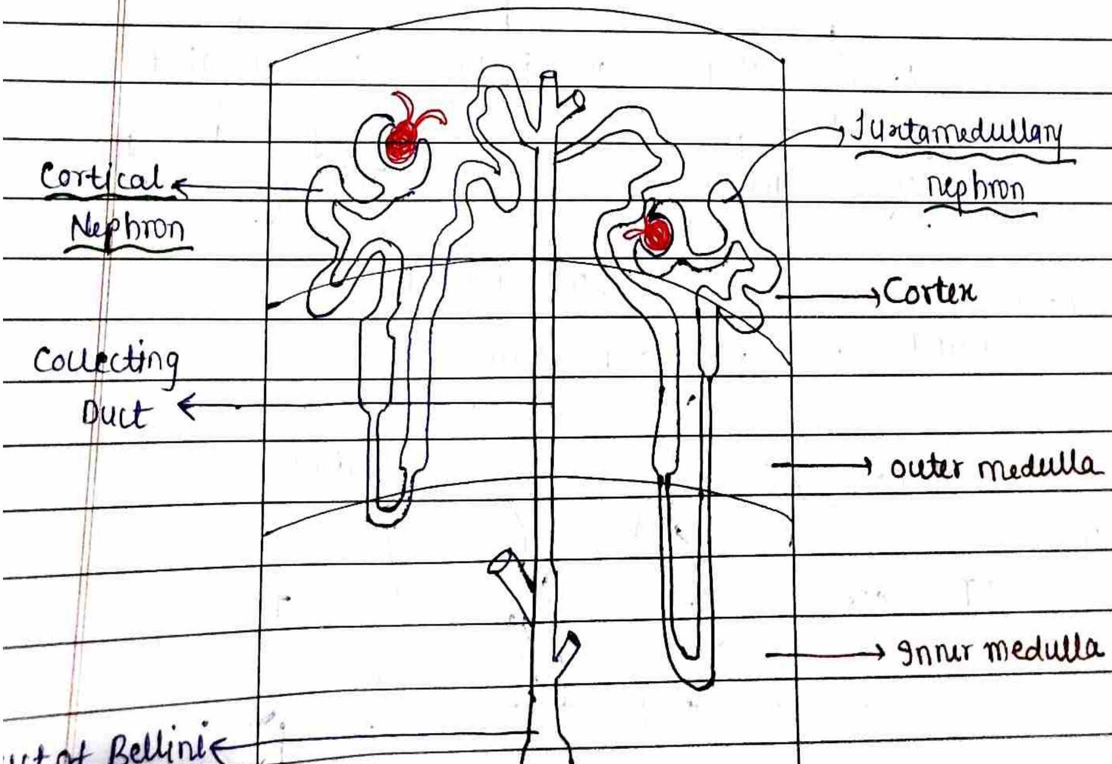

Efferent Arteriole
Afferent Arteriole
Glomerulus
DCT
PCT
Cortex
Thick seg.
Thick seg.
Outer Medulla
Collecting duct
Thin seg.
Thin seg
Hairpin bend
Inner Medulla

OPPO A53
2022/07/ 15:22:38

Date
Page

☆ Types of Nephron

Features	Cortical Nep.	Juxtamedullary Nep.
%	85%	15%
Situation of Renal corpuscle	Outer cortex near periphery	Inner cortex near medulla
Loop of Henle	Short	Long
Blood supply	Peritubular capillaries	Vasa Recta
Function	form^n of urine	mainly conc. of urine & form^n of urine also


Juxtamedullary nephron
Cortical Nephron
Cortex
Collecting Duct
outer medulla
Inner medulla
uct of Bellini

OPPO A53

Date ....
Page ....

② JUXTAGLOMERULAR APPARATUS

→ Specialized organ situated near the glomerulus of each nephron.

★ Structure

formed by 3 diffⁿ structures

1. Macula densa
2. Extraglomerular mesangial cells
3. Juxtaglomerular cells

a) Macula Densa

→ End portion of thick ascending segment situated b/w afferent & efferent arteriole.

→ Formed by tightly packed cuboidal epithelial cells.

→ Imp. role in Tubulo-glomerular feedback mechanism

→ Secretes Thromboxane A_2

b) Extraglomerular Mesangial cells

→ Situated in Δ region b/w afferent, efferent arteriole & macula densa.

→ Also c/d Agranular cells, Lacis cells

→ Secretes Prostaglandins & cytokines

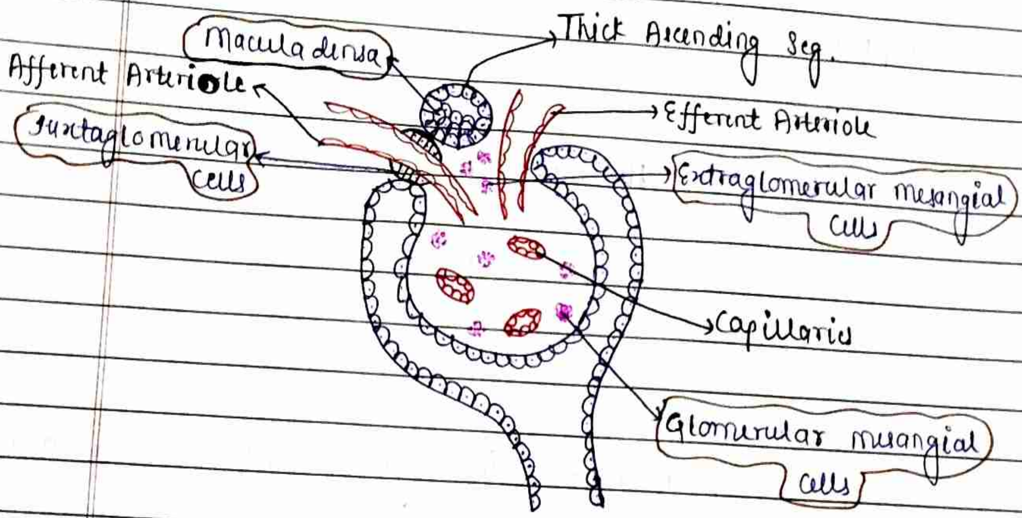
c) Juxtaglomerular cells

→ Specialized smooth muscle cells situated in wall of afferent arteriole b/w Tunica media & Tunica Adventitia before it enters the Bowman's Capsule.

→ Also c/d Granular cells (contains secretory granules)

OPPO A53
2022/07/15 22:38

Polar cushion / Polkissen → JG cells forms a thick cuff c/d Polkissen around afferent arteriole.


Macula densa
Thick Ascending Seg.
Afferent Arteriole
Efferent Arteriole
Juxtaglomerular cells
Extraglomerular mesangial cells
Capillaries
Glomerular mesangial cells

★ functions of JG Apparatus

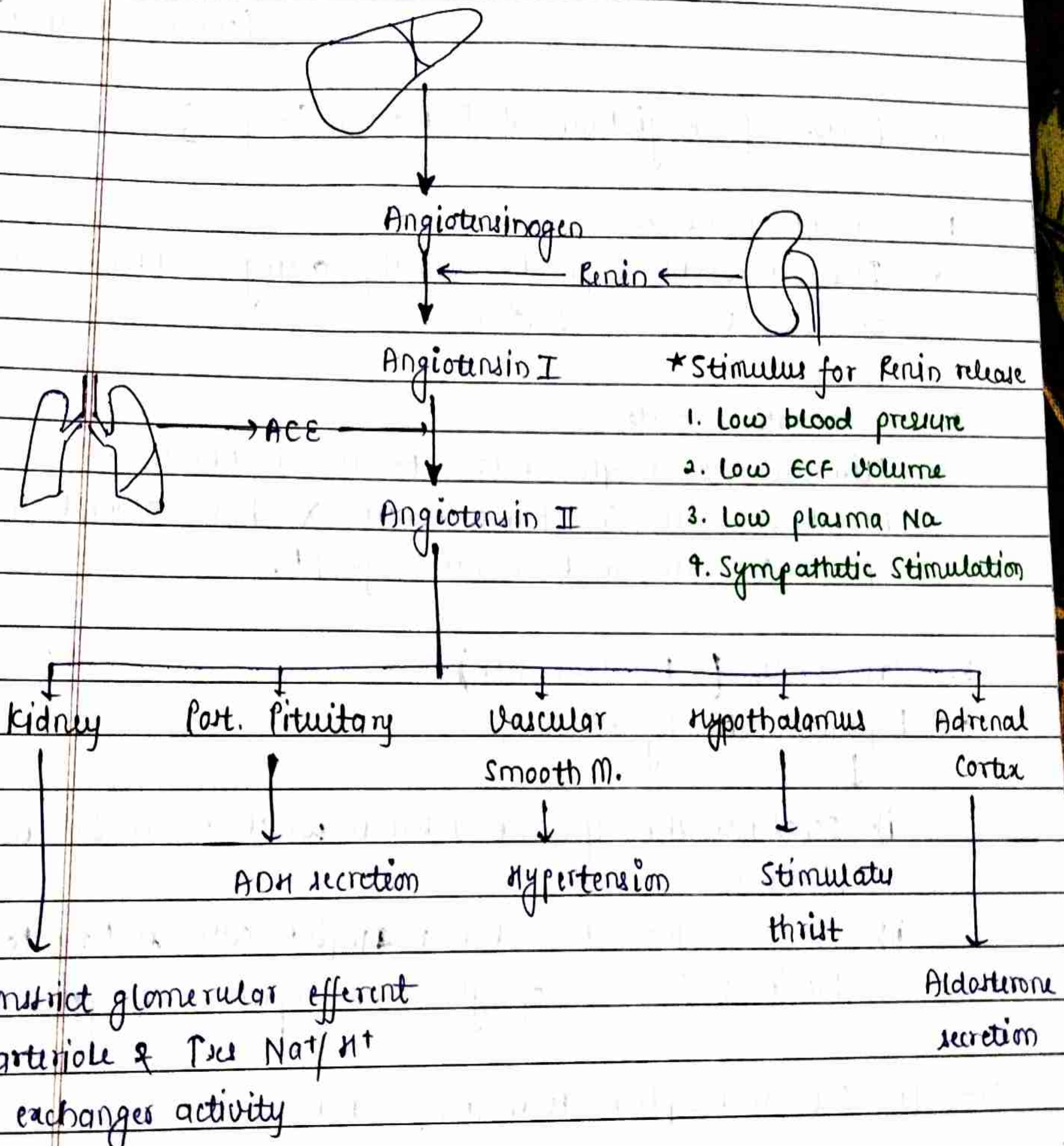
① Secretion of Hormones
→ Renin
→ Prostaglandins

a) Renin
→ JG cells secretes Renin
→ Along with Angiotensins, forms the Renin-Angiotensin System.

OPPO A53

Most imp

Renin – Angiotensin System


Angiotensinogen
Renin
Angiotensin I
ACE
Angiotensin II
Kidney
Post. Pituitary
Vascular Smooth M.
Hypothalamus
Adrenal Cortex
ADH secretion
Hypertension
Stimulates thirst
Aldosterone secretion
Constrict glomerular efferent arteriole & ↑ses Na+/H+ exchanger activity

★Stimulus for Renin release

1. Low blood pressure
2. Low ECF volume
3. Low plasma Na
4. Sympathetic Stimulation

→ when renin is released into blood

↓

acts on specialised plasma protein Angiotensinogen (α_2 globulin)

↓

By renin, angiotensinogen converts into Angiotensin I

↓

OPPO A53
2022/07/15 22:38

Angiotensin I is converted to Angiotensin II by ACE
↓
(secreted from lungs)

* Actions of Angiotensin II [most Active form]

1. On blood vessels

→ ↑ses arterial blood pr. by directly acting on blood vessels and caused vasoconstriction.

2. On adrenal cortex

→ Stimulates zona-glomerulosa to secrete Aldosterone

→ Aldosterone acts on Renal Tubule & ↑ses absorption of Na & water and excretion of K⁺.

3. On kidney (Regulates GFR)

→ Regulates GFR by 2 ways
↓

i) Constricts the efferent Arteriole which causes ↓se in filteration

ii) Contracts the glomerular mesangial cells leading to ↓se in surface area of glomerular capillaries & filteration

→ ↑se Na reabsorption from renal tubules.

4. On Brain

→ Inhibits Baroreceptor reflex & indirectly ↑es BP.
↓
(↓ses BP)

→ Stimulates Thrist center

→ ↑se secretion of CRH from Hypothalamus which causes ↑se

OPPO A53
2022/07 5:22:39

secretion of ACTH from pituitary.

→ The secretion of ADH from hypothalamus

5. Other actions

→ Acts as a growth factor in heart causing muscular hypertrophy & cardiac enlargement

b) Prostaglandins

→ Extraglomerular mesangial cells secretes Prostaglandins,

→ Also secreted from Type I medullary Interstitial cells.

② Secretion of other Substances

→ Extraglomerular mesangial cells secretes → cytokines like IL-2

→ Macula densa secretes ⟶ Thromboxane A_2

③ Regulation of Glomerular Blood flow & GFR

→ Macula densa of JG apparatus plays an imp. role in Tubulo-Glomerular feedback mechanism, which regulates renal blood flow & GFR.

OPPO A53
2022/07/ 5 22:39

③ URINE FORMATION

→ It is a blood - cleansing function

→ Kidney excretes the unwanted substances along with water from blood as urine.

→ Urine output in a nrml person is 1 to 1.5 L/day.

★ Process of Urine formation

→ Includes 3 processes :-

- Glomerular fiteration
- Tubular Reabsorption
- Tubular Secretion

① Glomerular filteration

→ Process by which blood is filtered while passing through glomerular capillaries by fiteration membrane.

★ fiteration membrane :- 3 layers → 1. Glomerular Capillary mem.
2. Basement mem.
3. Visceral layer of Bowman's Capsule

- Glomerulus capillary Membrane

→ formed by single layer of Endothelial cells, attached to basement membrane.

→ Has many pores c/d fenestrae / filteration pores

- Basement Membrane

BM of glomerular capillary + BM of Bowman's capsule
↓
fused together & separates the endothelium of glomerular capillary & epithelium of visceral layer.

OPPO A53
2022/07/25 22:39

- Visceral layer of Bowman's Capsule

→ formed by single layer of flattened epithelial cell.

→ These cells connected with BM by cytoplasmic extensions c/d Pedicle, cells with pedicle are c/d Podocytes.

→ Pedicle leaves small cleft-like space in b/w c/d slit Pores/ filteration slit (site of fiteration).

★ Process of Glomerular fiteration

→ When blood passes through glomerulus capillaries

↓

plasma is filtered into Bowman's Capsule

↓

All sub. are filtered except Plasma Proteins

↓

filtered fluid is c/d Glomerular filterate

★ Ultrafilteration

→ Glomerular filteration is c/d ultrafilteration b/c even minute particle is filtered, but plasma proteins are not filtered due to their large molecular size.

→ Glomerular filterate contains all sub. ⊕nt in plasma except Plasma protein

most imp.

★ GLOMERULAR FILTERATION RATE (GFR)

→ Defined as total quantity of filterate formed in all the nephrons of both the kidney in given unit of time.

★ Nrml GFR is 125 ml/ min or 180 L/ day

→

- Fitteration Fraction

fraction of Renal plasma which becomes fitterate.

$$F.F. = \frac{GFR}{\text{Renal plasma flow}} \times 100 = \frac{125\ ml/min}{650\ ml/min} \times 100$$

$$= 19.2\%$$

OPPO A53
2022/07 15:10:39

Nml F.F. varies from 15 to 20%

- Pressures determining GFR
  1. Glomerular capillary pr.
  2. Colloidal Osmotic pr. ⟶ in glomeruli
  3. Hydrostatic Pr. ⟶ in Bowman's Capsule

① Glomerular capillary Pr. (favours Glomerular filteration)
→ Pr. exerted by blood in Glomerular Capillary.
→ It is about 60 mm Hg.
→ Highest capillary Pr. in body

② Colloidal Osmotic Pr. (opposes Glomerular filteration)
→ Pr. exerted by Plasma protein in Glomerular Capillary.
→ It is about 25 mm Hg.

③ Hydrostatic Pr. (opposes Glomerular filteration)
→ Pr. exerted by filterate in Bowman's Capsule.
→ Also cld Capsular Pr.
→ It is about 15 mm Hg

★ Net filteration Pressure
Balance b/w Pr. favouring & Pr. opposing filtration

$$NFP = \text{Glomerular Capillary Pr.} - \left[\text{Colloidal osmotic Pr.} + \text{Hydrostatic Pr. in Bowman's}\right]$$

$$= 60 - [25 + 15]$$

$$\boxed{NFP = 20 \text{ mm Hg}}$$

↓
Varies b/w 15 to 20 mm Hg

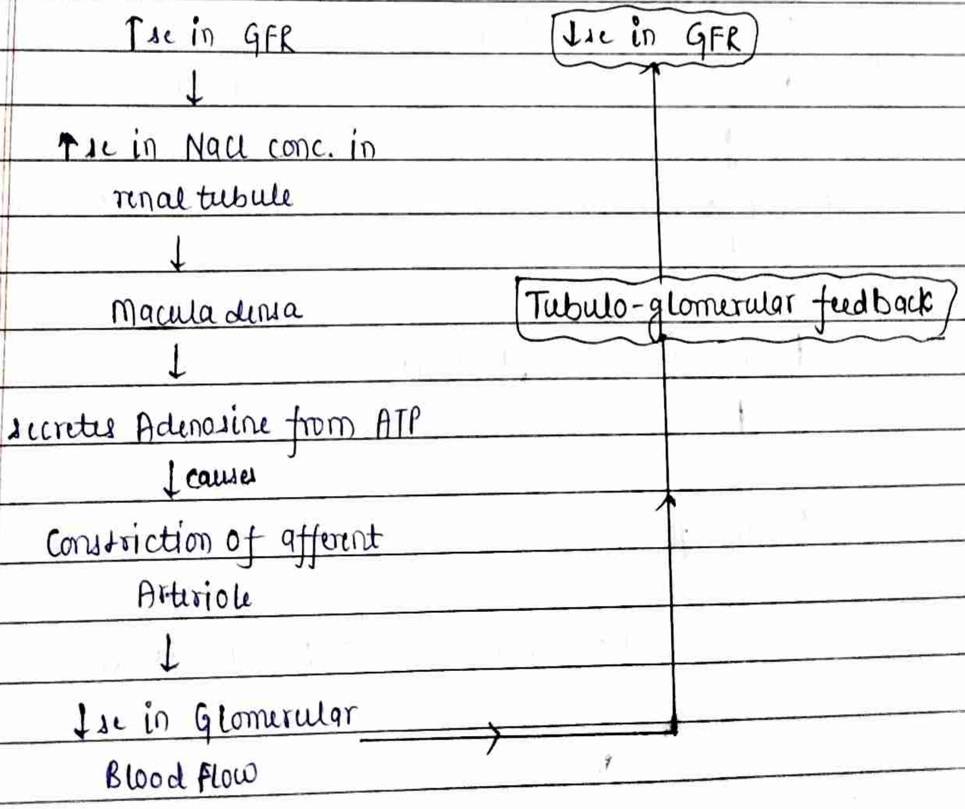
OPPO A53
2022/07/15 22:39

Date
Page

100* • Factors Regulating GFR

1. Renal Blood flow
→ Most imp. factor for Glomerular filteration
→ * GFR $\propto$ Renal Blood flow
→ Normal blood flow to both kidneys is 1,300 ml/min.

Imp. 2. Tubulo-Glomerular Feedback
→ Regulates GFR through renal tubules & macula densa
→ Macula densa → acts like a sensor & detects the conc. of
→ NaCl in tubular fluid & accordingly alters glomerular blood flow & GFR.


↑se in GFR
↑se in NaCl conc. in renal tubule
Macula densa
secretes Adenosine from ATP
causes
Constriction of afferent Arteriole
↓se in Glomerular Blood Flow
↓se in GFR
Tubulo-glomerular feedback

When conc. of NaCl ↑ses in filterate

OPPO A53
2022/07/15 12:39

↓se in GFR

↓

↓se in NaCl conc. in renal tubule

↓

macula densa

↓

secretes Prostaglandins①, Bradykinin② & Renin③

↓

①+② causes → dilation of afferent arteriole

↓

③ causes → formn of Angiotensin II
• which causes constriction of efferent arteriole

↓

finally dilation of afferent + constriction of efferent leads to

↓

↑se in Glomerular Blood flow

↓

↑se in GFR

when conc. of NaCl ↓ses in filtrate

3. Glomerular capillary Pr.

→ GFR ∝ Glomerular capillary Pr.

→ when capillary Pr. ↑ses, GFR ↑ses

OPPO A53
2022/07

Date
Page

4. Colloidal Osmotic Pr.

$$GFR \propto \frac{1}{\text{Colloidal Osmotic Pr.}}$$

In dehydration → COP ↑ses, GFR ↓ses
In hypo-proteinemia → COP ↓ses, GFR ↑ses

5. Hydrostatic Pr. in Bowman's capsule

$$GFR \propto \frac{1}{\text{Hydrostatic Pr.}}$$

↓

- ↑ses in condn like obstruction of urethra, edema of kidney.

6. Constriction of Afferent Arteriole

Reduces flow of blood & thus ↓ses GFR.

7. Constriction of Efferent Arteriole

↑ses the GFR initially b/c of stagnation of blood in capillaries.

8. Systemic Arterial Pr.

→ when arterial blood Pr. is in b/w 60 to 180 mm Hg

↓

Renal Blood flow & GFR remains unaffected.

→ Variation of Pr. above 180 mm Hg or below 60 mm Hg

↓

Affects Renal Blood flow & GFR

↓ b/c

Autoregulatory mechanism fails beyond this range.

OPPO A53
2022/07 5:22:30

Date
Page

9. **Sympathetic Stimulation**

→ Afferent & Efferent arteriole → supplied by Sympathetic Nerves

→ Mild or Moderate stimulation → No effect on GFR

→ Strong stimulation → causes severe constriction by releasing NT (nor-adrenaline)

↓

initially ↑se in GFR but later it decreases b/c

↓

constriction prevents outflow of blood from glomerulus & no fresh blood enters the glomerulus for filteration

10. **Surface Area of Capillary Membrane**

→ GFR ∝ Surface Area

→ If mem. affected as in renal diseases

↓

SA ↓ses

↓

GFR ↓ses

11. **Permeability of Capillary Membrane**

→ GFR ∝ Permeability of CM

→ In abnormal condn like Hypoxia, Lack of Blood supply, presence of toxic agents

↓

Permeability ↑ses

↓

Even plasma proteins are filtered & excreted in urine

OPPO A53
2022/07/15 22:39

12. Constraction of Glomerular Mesangial cells

→ Situated in b/w glomerular capillary

→ contraction of these cells → ↓se SA of capillaries

↓

↓se in GFR

13. Hormonal & other factors

→ Factors ↑sing GFR by vasodilation → 1. ANP (Atrial Natriuretic Peptide)

2. BNP (Brain ——〃——)

3. cAMP

4. Dopamine

5. Prostaglandins E_2

→ Factors ↓sing GFR by vasoconstriction → 1. Angiotensin II

2. Endothelin

3. Nor-adrenaline

4. Platelet Activating factor

5. Prostaglandins F_2

② Tubular Reabsorption

→ Process by which water & other substances are transported from renal tubule back to blood.

filterate in tubular portion of nephron

↓

electrolyte & other sub. reabsored by tubular epithelial cells

↓

Sub. move into Interstitial fluid of renal medulla

↓

Finally sub. move into blood in peritubular capillaries

OPPO A53
2022/07

Since the sub. are taken back into the blood from glomerular filtrate, the entire process is c/d Tubular Reabsorption.

★ Selective Reabsorption

→ Tubular reabsorption is k/n as Selective reabsorption b/c tubular cells reabsorb only the substances necessary for the body.

→ Sub. such as glucose, amino acid & vitamins are completely reabsorbed.

★ Mechanism of Reabsorption

→ 2 types

1. Active Reab.

→ Movement of molecule against electrochemical gradient.

→ Needs liberation of energy (derived from ATP)

Substances reabsorb Actively

Na, Ca, K, PO_4^{3-}, Bicarbonates, Glucose, A.A.

2. Passive Reab

→ Movement of molecule along the electrochemical gradient.

→ Does not need energy.

Substances reabsorb passively

Cl, Urea & water

OPPO A57

★ Routes of Reabsorption

→ By 2 routes

1. Transcellular Route

→ Sub. move through cell

→ Path :- Tubular lumen

↓

Tubular cells

↓

Interstitial fluid

↓

Capillary

2. Paracellular Route

→ Sub. move through Intercellular space

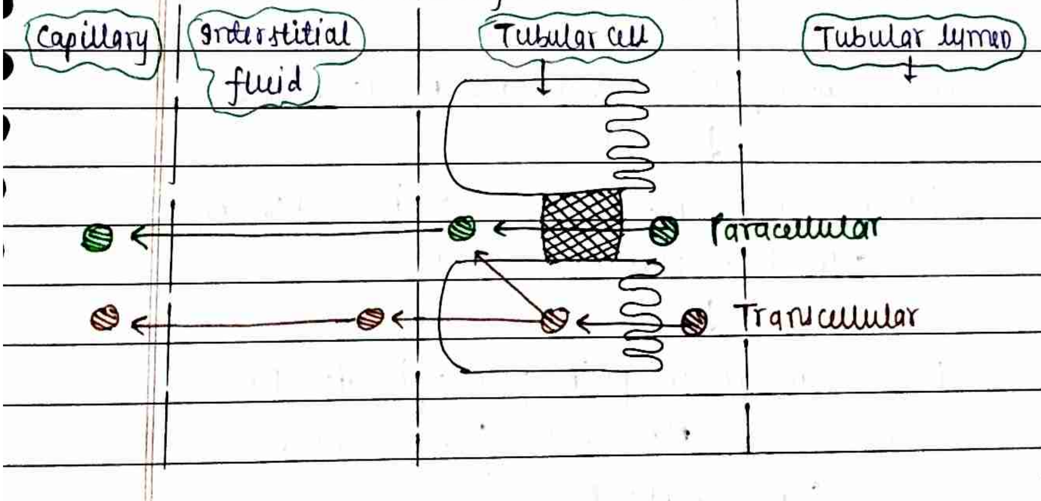
→ Path :- Tubular lumen

↓ ⟶ through tight junction b/w the cells

Interstitial fluid

↓

Capillary


Capillary
Interstitial fluid
Tubular cell
Tubular lumen
Paracellular
Transcellular

★ Regulation of Tubular Reabsorption

→ By 3 factors

1. Glomerulo-Tubular Balance
2. Hormonal factors
3. Nervous factors

OPPO A53
2022/07/15 22:39

Imp
① Glomerulo - Tubular Balance

→ Balance b/w filteration & reabsorption of solutes & water in kidney.

→ GFR increases

↓

Tubular load of solute & water in tubules ↑ses

↓

↑se in reabsorption of solutes & water

↓

helps in const. reabsorption of Na^+ & water from Renal tubule

Mechanism :- • Occurs b/c of osmotic pr. in peritubular capillaries

GFR ↑ses

↓

more plasma proteins accumulates in glomerulus

↓ leads to

↑se in osmotic pr. in blood as it reaches efferent arteriole & peritubular capillaries

↓

↑se osmotic pr. in peritubular capillaries ↑ses reabsorption of Na & water from tubule into capillary blood.

② Hormonal factors

- Aldosterone → ↑se Na^+ reabsorption
- Angiotensin II → ——"—————— mainly in PCT
- ANF → ↓se ——"———

OPPO A53
2022/07/15 22:3

- ADH → ↑se water reabsorption in DCT & collecting duct.
- Parath-Hr. → ↑se reabsorption of Ca, Mg & H
  - ↓se ——"—— Phosphate
- Calcitonin → ↓se reabsorption of Ca.

3. Nervous factors

→ Activation of Sympathetic Nervous System

↓

↑se tubular reabsorption from tubules

Imp. ★ **Transport Maximum – Tm Value**

→ Rate at which maxm amount of sub. is reabsorbed from Renal tubule

→ For every actively reabsorbed sub. there is a maxm rate at which it could be reabsorbed.

Ex :- Tm for Glucose is 375 mg/dl (in male)
300 mg/dl (in female)

★ Threshold level in Plasma for sub. having Tm value

→ Renal threshold is plasma conc. at which sub. appears in urine.

→ Every sub. having Tm value also has a threshold level in plasma / blood

→ Below Threshold level → sub. is completely reabsorbed & does not appear in urine.

→ When conc. reaches to Threshold → Excess amount is not reabsorbed.
So, it appears in urine

OPPO A53
2022/07/15 22:30

Ex:- Renal Threshold for glucose = 180 mg/dl

when conc. in blood is below 180 mg/dl → completely reabsorbed & does not appear in urine.

when blood level of glucose reaches 180 mg/dl → Not reabsorbed completely & appears in urine.

★ Reabsorption of Imp. Substances

Imp.

① Reabsorption of sodium (99% reabsorbed)

→ In PCT → 2/3rd

→ In other segments (except descending limb) → 1/3rd

★ Occurs in 3 steps :-

a) Transport from lumen of renal tubules into tubular epithelial cells

→ Occurs actively by 2 ways :-

- In PCT → in exchange for H^+ by antiport
- In other seg. & collecting Duct → along with glucose & AA. by symport

b) Transport from tubular cells into the interstitial fluids

→ Na is pumped outside the cell by $Na^+ - K^+$ Pump.

→ Pump moves ⟶ 3 Na^+ from cell into interstitium
2 K^+ from interstitium into cell

OPPO A53
2022/07/15 22:39

Transport of Na^+ out of tubular cells by pump, ↓ses the

Na+ conc. within the cell which

↓

develops an Electrochemical gradient b/w lumen & tubular cells

↓

results in diffusion of Na+ into cell

c) Transport from Interstitial fluid to blood.
From interstitial fluid, Na+ enters the peritubular capillaries by conc. gradient.

Imp.
② Reabsorption of Water
→ occurs in PCT, DCT & in collecting duct.

a) Reabsorption from PCT → obligatory water reabsorption
→ Type of water reabsorption from PCT, which is 2° (obligatory) to Na reabsorption.
→ when Na+ reabsorbed

↓

osmotic pr. ↓ses

↓

causes osmosis of water from renal tubule

b) Reabsorption of water from DCT & collecting Duct → facultative water reabsorption

→ Type of water reabsorption in DCT & CD that occurs by activity of ADH
→ Normlly, DCT & CD → impermeable to water
→ In presence of ADH, DCT & CD → permeable to water so reabsorbed

OPPO A53
2022/07/15 22:42

Na^+ conc. within the cell which

↓

develops an electrochemical gradient b/w lumen & tubular cells

↓

results in diffusion of Na^+ into cell

c) Transport from Interstitial fluid to blood.
From interstitial fluid, Na^+ enters the peritubular capillaries by conc. gradient.

Imp

② Reabsorption of Water

→ occurs in PCT, DCT & in collecting duct.

a) Reabsorption from PCT → obligatory water reabsorption

→ Type of water reabsorption from PCT, which is 2° (obligatory) to Na reabsorption.

→ when Na^+ reabsorbed

↓

osmotic pr. ↓ses

↓

causes osmosis of water from renal tubule

b) Reabsorption of water from DCT & collecting Duct → facultative water reabsorption

→ Type of water reabsorption in DCT & CD that occurs by activity of ADH

→ Nomlly, DCT & CD → impermeable to water

→ In presence of ADH, DCT & CD → permeable to water so reabsorbed

OPPO A53

④ CONCENTRATION OF URINE

** COUNTERCURRENT MECHANISM

→ Responsible for the development and maintainance of medullary gradient and hyperosmolarity of interstitial fluid in the inner medulla.

→ System of U-shape tubule in which the flow of fluid is in opp. direⁿ in 2 limbs of U-shaped tubules.

- Division of countercurrent System

Has 2 divisions :- 1. Countercurrent multiplier $\xrightarrow{\text{formed by}}$ loop of Henle
2. —"— Exchanger —"→ Vasa Recta

1. Countercurrent Multiplier (Produce conc. gradient)

→ loop of Henle functions as CM.

→ Responsible for development of hyperosmolarity of medullary interstitial fluid and medullary gradient.

* Role of Loop of Henle in development of Medullary Gradient

→ Loop of Henle of juxtamedullary nephron plays a major role as CM b/c loop of Henle of these nephrons are very long & extend upto depper part of medulla.

- Descending limb of LOH → Highly Permeable to H_2O
  Impermeable to solutes

→ As fluid flows down, it becomes increasingly hypertonic as water is selectively removed.
fluid at tip is highly concentrated & osmolarity is more then interstitial osmolarity.

OPPO A53

Thin
- Ascending limb of LOH → Permeable to solute
  Impermeable to water

→ As fluid goes up, solutes are passively transported from the hypertonic tubular fluid into interstitium.

→ Everytime the tubular fluid passes through this thin limb extra solutes enter the interstitium.

↓

this help in multiplication of interstitial osmolarity

- Thick Ascending limb of LOH → Permeable to solute
  Impermeable to water

→ Na^+ & Cl^- are actively transported from tubular fluid due to activity of Na^+-K^+ ATPase

→ This aids in building up of higher interstitial osmolality

2. Countercurrent Exchanger (Maintains conc. gradient)

→ Vasa recta functions as CE.

→ NaCl & Urea accumulated in interstitium are removed by circulation.

- In the descending limb of Vasa recta / vessel
  Solute diffuse into vessel that is carrying blood into medullary pyramid.

- In the ascending limb of Vasa recta
  Solute diffuses out of vessels that is carrying blood toward cortex.

OPPO A53
2022/07/15 22:53

- Solutes keep circulating in interstitium

- Movement of water is opp. to movement of solutes

↓

Water diffuses out of descending limb & into the ascending limb of vasa recta

↓

Water in vasa recta enters general circulation & helps in maintaining ECF volume

3. Role of Collecting Duct (acts as osmotic equilibrating device)

→ Contributes to urine conc. by 2 ways :-

- CD is permeable to water → water moves out from CD into hyperosmolal interstitium both in cortical & medullary part.

↓

this makes urine hypertonic

- Urea transported in CD → Except in inner medullary portion of CD, rest of tubular epithelium is relatively impermeable to urea.

→ Some urea is secreted into descending limb of LOH

↓

as fluid reaches medullary part of CD, its urea conc. is very high

↓

So, urea moves from tubular fluid into interstitium passively

↓ result

water also moves out of tubular lumen along with urea to maintain osmotic balance

↓

Thus, urine is more concentrated

→ Water that enters interstitium is taken up by vasa recta & thus osmolal dilution of interstitium is prevented.

OPPO A53
2022/07/15 22:53

★ NET EFFECT

→ Every time fluid passes through LOH

↓

water • comes out ⟶ from descending limb into interstitium

• removed by ⟶ ascending limb of Vasa Recta

Solute • comes out ⟶ from ascending limb ~~limb~~ into inter-stitium

↙ diffuses passively in thin ascending portion

↘ pumped actively in thick ascending portion

• removed by ⟶ descending limb of vasa recta

→ Longer LOH accumulates more solute across it from outer to deep layers of medulla.

↓

thus osmolality ↑es along LOH as it dips into medulla

↓ result

higher osmolality in medullary interstitium

↓

further enhanced by diffusion of urea from CD due to which

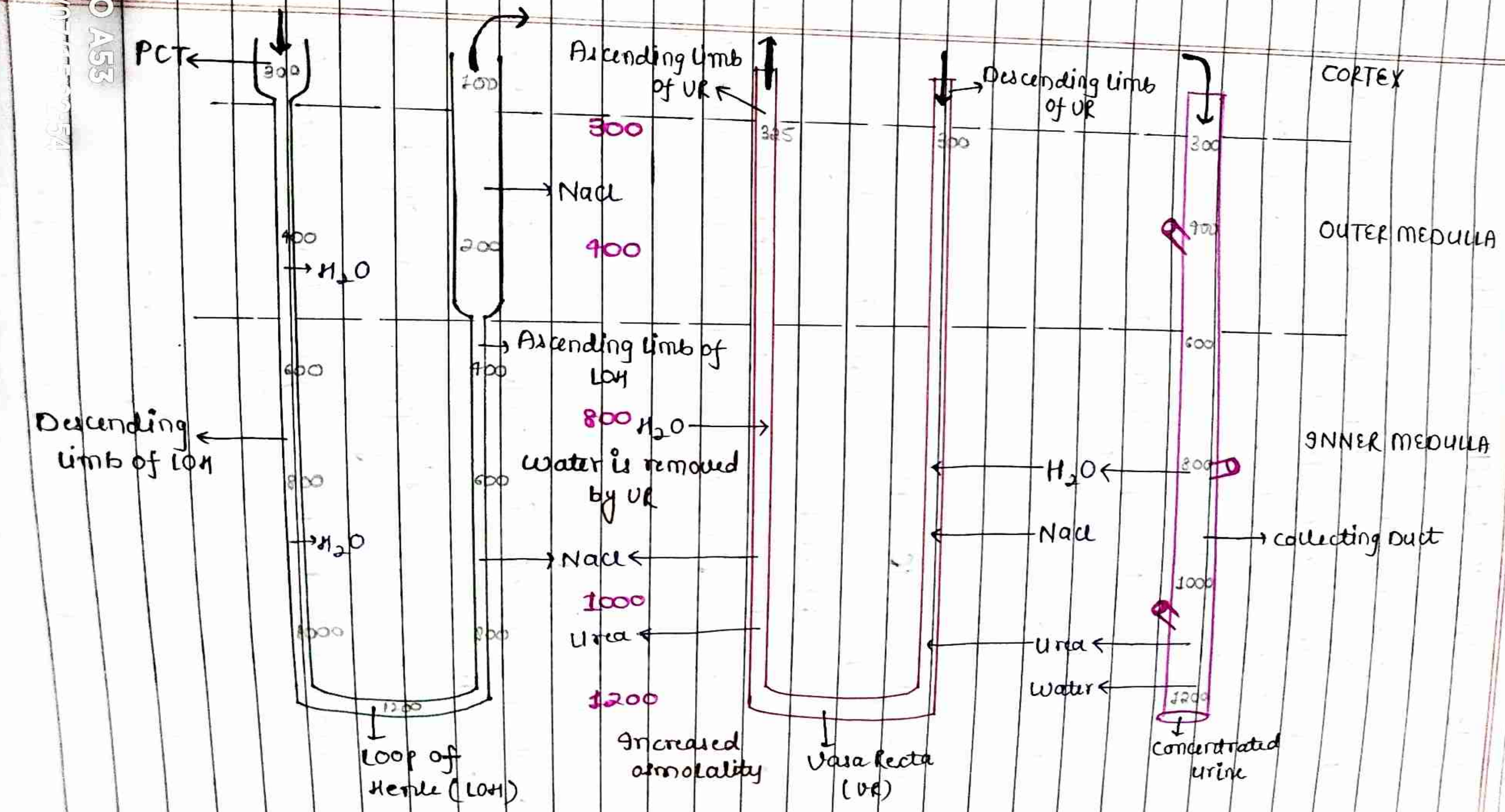
↓

water also moves out passively from CD but removed by vasa recta.

Result :- • Osmolality of about 1200 - 1400 mosmol/Kg of H_2O is maintained in deep medulla.

• This high osmolality causes transfer of H_2O from CD & makes urine concentrated.

OPPO A53
2022/07/1 2:54


PCT
300
100
200
400
H_2O
600
700
Descending limb of LOH
800
H_2O
1000
1200
Loop of Henle (LOH)
NaCl
Ascending limb of LOH
600
800
NaCl
Ascending limb of VR
300
400
800
H_2O
water is removed by VR
1000
Urea
1200
Increased osmolality
325
Vasa Recta (VR)
Descending limb of VR
300
H_2O
NaCl
Urea
Water
CORTEX
OUTER MEDULLA
INNER MEDULLA
300
400
600
800
1000
1200
collecting Duct
concentrated urine

OPPO A53

Date
Page

⑤ ROLE OF KIDNEY IN ACID BASE BALANCE

→ Kidney plays an imp. role in maintainance of acid-base balance by excreting H^+ ions & retaining HCO_3^- ions.

→ Metabolic activities in the body produces large quantity of acids (with excess of H^+), which try to push the body towards acidosis

↓

Kidney prevents this by

Reabsorption of HCO_3^- ions | Secretion of H^+ ions

a) Reabsorption of HCO_3^- ions

→ About 4,300 of HCO_3^- ions is filtered by glomeruli every-day, i.e filtered load.

→ Excretion of this much HCO_3^- will affect the acid-base balance of body, so HCO_3^- must be taken back by reabsorption.

b) Secretion of H^+ ions

→ Reabsorption of HCO_3^- ions occurs by secretion of H^+ into the renal tubule

→ About, 4,380 mEq of H^+ appears every day in renal tubule

↓

About 4,280 to 4,330 mEq of H^+ is utilized for reabsorption of HCO_3^-

↓

Remaining 80 to 100 mEq is excreted

↓

Results in acidification of urine

OPPO A53
2022/07/15 22:54

→ Secretion of H^+ occurs by 2 pumps :- 1. Sodium-H^+ Antiport
2. ATP driven proton pump

1. Na^+- H^+ Antiport Pump [occurs in PCT]

→ Occurs in PCT

→ Na^+ → reabsorbed from tubular fluid into tubular cell
H^+ → secreted from tubular cell into tubular fluid
↓
In exchange of Na^+

2. ATP- Driven Proton Pump [occurs in DCT & CD]

→ Additional pump for H^+ secretion in DCT & CD.

★ Removal of H^+ ions & Acidification of Urine
Occurs by 3 mechanism :- 1. Bicarbonate Mechanism
2. Phosphate —— " ——
3. Ammonia —— " ——

① Bicarbonate Mechanism [occurs in PCT, LOH & DCT]

→ All the filtered HCO_3^- in renal tubule is reabsorbed
↓
80% in PCT | 15% in LOH | 5% in DCT & CD

→ Reabsorption requires H^+

Mechanism:- H^+ in renal tubule [lumen]
↓
$$H^+ + HCO_3^- \rightarrow H_2CO_3$$
↓
$$H_2CO_3 \xrightarrow{CA} \underbrace{H_2O + CO_2}_{\text{Enters tubular cells}}$$
↓

OPPO A53
2022/07/15 22:54

In tubular cell :- $CO_2 + H_2O \rightarrow H_2CO_3$

↓

$H_2CO_3 \rightarrow H^+ + \underbrace{HCO_3^-}$

↓ enter the interstitium

Simultaneously, Na^+ reabsorbed from tubular lumen

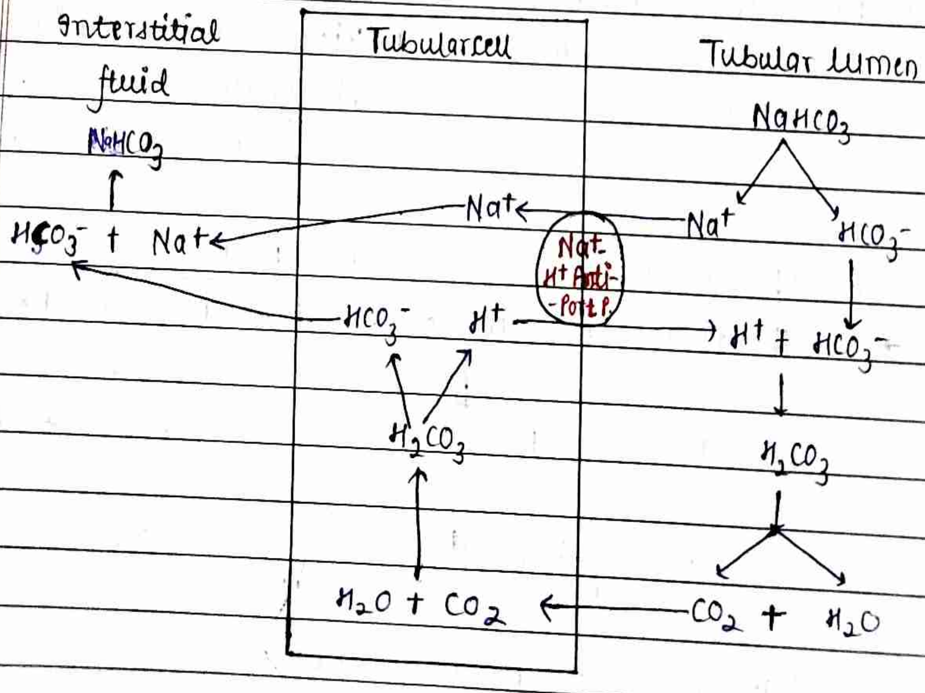
↓

$HCO_3^- + Na^+ \rightarrow NaHCO_3$ in Interstitium

↓

H^+ secretes in lumen in exchange of Na^+

∴ For every H^+ secreted into lumen → 1 HCO_3^- is reabsorbed from tubule into interstitium


Interstitial fluid
$NaHCO_3$
$HCO_3^- + Na^+$
Tubular cell
Na^+
HCO_3^-
H^+
H_2CO_3
$H_2O + CO_2$
Na^+ H^+ Anti-Port P.
Tubular lumen
$NaHCO_3$
Na^+
HCO_3^-
$H^+ + HCO_3^-$
H_2CO_3
$CO_2 + H_2O$

*Reabsorption of HCO_3^- ion by secretion of H^+ in renal tubule

OPPO A53

② Phosphate Mechanism [occurs in DCT & CD]

→ $CO_2 + H_2O \xrightarrow[\downarrow]{} H_2CO_3$

in tubular cell

↓

$H_2CO_3 \longrightarrow H^+ + \underbrace{HCO_3^-}_{\downarrow}$

↓ enters the interstitium

Simultaneously, Na^+ is reabsorbed by Na^+-H^+ antiport pump

↓

H^+ secreted in lumen in exchange of Na^+

↓

H^+ in lumen reacts with phosphate buffer

↓

$H^+ + NaHPO_4 \longrightarrow NaH_2PO_4$

(Sodium Hydrogen Phosphate) (Sodium Dihydrogen Phosphate)

↓

- excreted in urine
- H^+ in it makes the urine acidic
- occurs in DCT & CD b/c they contain large quantity of $NaHPO_4$.

③ Ammonia Mechanism [occurs in PCT]

→ Most imp. mechanism by which kidney excretes H^+ & makes urine acidic.

→ In tubular cell :- • Glutamine $\xrightarrow[\text{converts into}]{\text{Glutaminase}}$ Glutamic Acid + $\boxed{NH_3}$

- Also formed by deamination of Glycine & Alanine A.A.

OPPO A53
2022/07/15 12:54

NH_3 in tubular cell

↓

Secretes in lumen in exchange for Na^+

↓

$NH_3 + H^+ \longrightarrow NH_4$

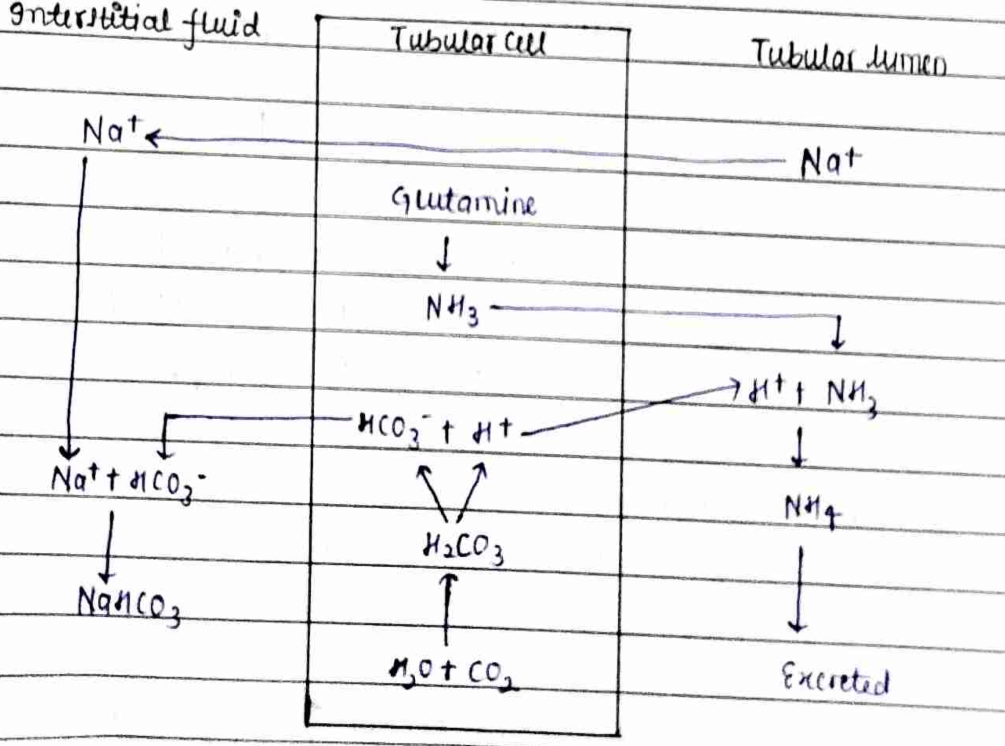
in lumen

↓

Tubular cell mem is impermeable for NH_4 so it remains in lumen & excretes in urine

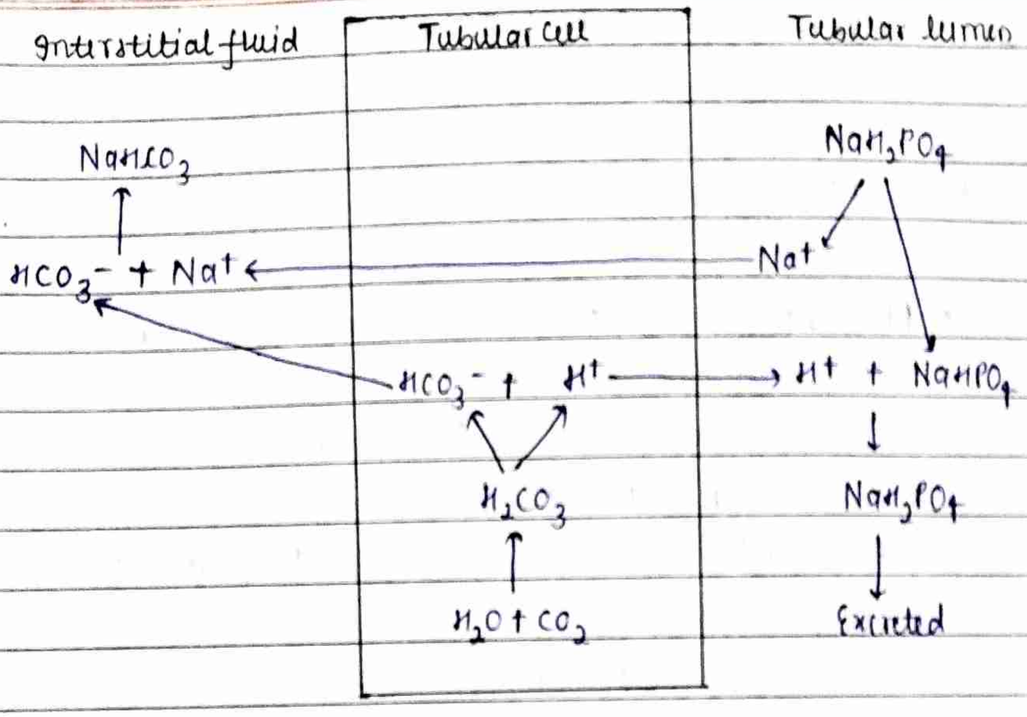
↓

∴ H^+ added to urine in form of NH_4 & causes acidification of urine


Interstitial fluid
Tubular cell
Tubular lumen
Na+
Na+
Glutamine
NH3
H+ + NH3
HCO3- + H+
Na+ + HCO3-
NH4
H2CO3
NaHCO3
H2O + CO2
Excreted

*Excretion of H^+ in combination with NH_3

OPPO A53
2022/07/15 22:55


Interstitial fluid
Tubular cell
Tubular lumen
$NaHCO_3$
$HCO_3^- + Na^+$
Na^+
NaH_2PO_4
$HCO_3^- + H^+$
$H^+ + NaHPO_4$
H_2CO_3
NaH_2PO_4
$H_2O + CO_2$
Excreted

*Excretion of H^+ in combination with sodium Hydrogen Phospate

OPPO A53

⑥ RENAL FUNCTION TEST

★ Examination of Blood & Urine

- **PLASMA CLEARANCE** (also k/n as Renal Clearance)

→ Defined as the amount of Plasma that is cleared off a sub. in a given unit of time.

→ Based on ficks law / Principle

→ Determination of clearance value help in assessing following renal function :-

1. GFR
2. Renal plasma flow
3. Renal Blood flow

$$\boxed{C = \frac{UV}{P}}$$

C = Clearance
U = conc. of sub. in urine
V = vol. of urine flow
P = Conc. of sub. in plasma

a) Measurement of GFR

→ Sub. that is completely filtered but neither absorbed nor secreted is used to measure GFR.

→ Inulin → • Ideal sub. to measure GFR
• Completely filtered, neither absorbed nor secreted

OPPO A53
2022/07

Imp. **Inulin Clearance**

- Known amount of Inulin is injected into body.
- After some time, conc. of Inulin in plasma & urine & vol. of urine excreted are estimated.

Ex:- Conc. of inulin in urine = 125 mg/dl
—— " —— plasma = 1 mg/dl
Vol. of urine output = 1 ml/min

$$GFR = \frac{UV}{P} = \frac{125 \times 1}{1}$$

$$= 125 \text{ ml/min}$$

- Creatinine clearance is also used

b) Measurement of Renal Plasma flow

- Sub. that is filtered & secreted but not reabsorbed, is used to measure Renal Plasma flow.

Para-Amino Hippuric Acid (PAH) → • Ideal sub.

PAH Clearance

- Indicates the amount of plasma passed through kidney
- known amount of PAH is injected into body.
- same line as of Inulin

Ex:- Conc. of PAH in urine = 66 mg/dl
—— " —— Plasma = 0.1 mg/dl
Vol. of urine output = 1 ml/min

$$\text{Renal plasma flow} = \frac{UV}{P} = \frac{66 \times 1 \times 10}{0.1}$$

$$= 660 \text{ ml/min}$$

OPPO A53
2022/07/15 22:55

c) Measurement of Renal Blood Flow

→ factors necessary to determine Renal Blood flow are :-

1. Renal Plasma Flow

   already done above

2. % of Plasma volume in Blood

   - Indirectly determined by using PCV
   - If PCV = 45%

     then, Plasma Vol. = 100 - 45 = 55%

     $\downarrow$

     i.e., 55 ml plasma is ⊕nt in every 100 ml of blood.

★ Calculation of Renal Blood flow

$$\text{Renal Blood flow} = \frac{\text{Renal Plasma flow}}{\text{\% of Plasma in blood}}$$

$$= \frac{660}{55/100} = \frac{\overset{6}{\cancel{660}} \times \overset{20}{\cancel{100}}}{\underset{5}{\cancel{55}}}$$

$$= 1,200 \text{ ml/min}$$

OPPO A53
2022/07/15 09:55

⑦ MICTURATION

** CYSTOMETROGRAM

→ Technique used to study the relationship b/w intravesicle pressure & volume of urine in bladder.

→ Graphical recording of pressure change in urinary bladder in relation to volume of urine collected in it.

* Method of Recording

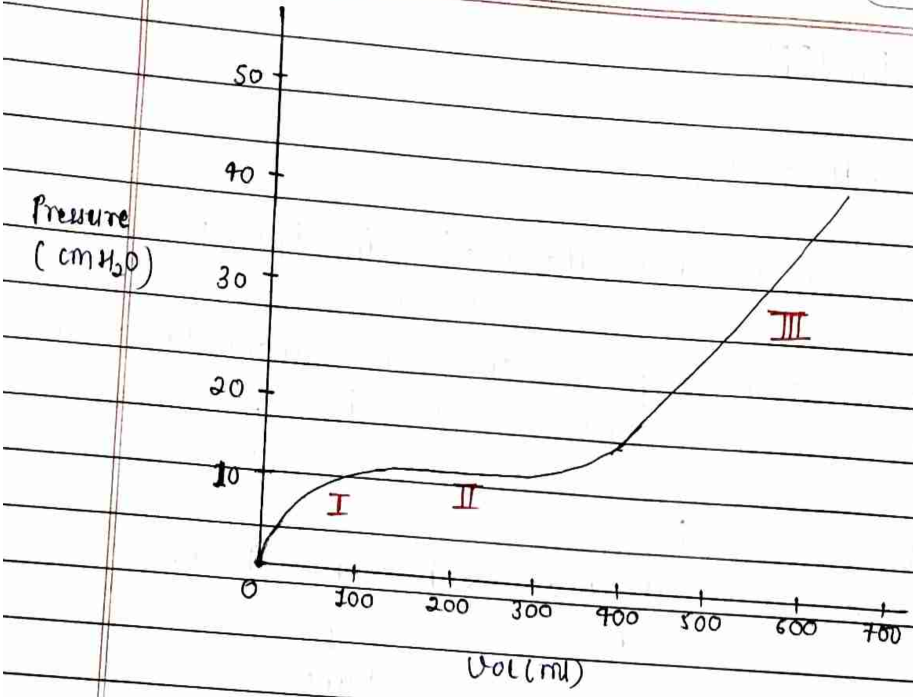
→ Double lumen catheter introduce in urinary bladder

Lumen 1
↓
used to infuse fluid into bladder.

Lumen 2
↓
Used to record the pressure changes by connecting to suitable recording instrument

Method :- first, Bladder is emptied completely
↓
K/n quantity of fluid is introduce into bladder at regular interval
↓
Intravesicle pr. is recorded continuously
↓
finally gr. is obtained b/w vol. & pressure

OPPO A53
2022/07/15 22:55



★ Segment I

Initially, when bladder empty, IV = 0
when 100 ml fluid collected, IV = 10 cm H_2O

★ Segment II (Plateau) → no change in IV pressure

→ Even after introducing 300 to 400 ml fluid, IV = 10 cm H_2O
↓
b/c of adaptation of bladder by relaxation

→ follows law of Laplace

$$\boxed{P = \frac{T}{R}}$$

P = Pr.
R = Radius
T = Tension

In bladder, T ↑ses as urine fills
R also ↑ses due to → relaxation of detrusor muscle

∴ P → does not change
∴ Plateau appears

OPPO A53

At, 100 ml of urine → desire for micturition occurs
> 400 ml —"— → pr. strats rising sharply

★ Segment III

→ As pr. ↑ses, contraction of muscle ↑ses.
→ At, 600 to 700 ml → pr. rises to 30 to 40 cm H_2O
→ when IV ↑ses beyond 40 cm H_2O
↓
Contraction of detrusor ms. become more intense
↓
Voluntary control is not possible
↓
Pain sensation develops & micturition is must

Most Imp.

★★ MICTURITION REFLEX

→ Reflex by which micturition occurs.
→ Elicits by stimulation of stretch receptors
↓
⊕nt on wall of bladder & urethra

→ At, 300 to 400 ml → IV pr. ↑ses
urine in bladder
↓
Stretches the wall of bladder
↓
Stimulation of stretch receptor
↓ results in
generation of sensory impulses

OPPO A53
2022/07/15 22:55

Date ________
Page ________

Filling of urinary bladder

↓

Stimulation of stretch receptors of urinary bladder

↓

Afferent impulses pass via pelvic (parasympathetic) N.

↓ reaches

Sacral segments of spinal cord

↓

Efferent impulses via pelvic Nerve

↓ causes

Contraction of detrusor muscle (bladder) &
relaxation of internal sphincter

↓

flow of urine into urethra and
stimulation of stretch receptors of urethra

↓

Afferent impulses via pelvic N.

↓ reaches spinal cord

Impulse generated from spinal cord

↓ causes

Inhibition of pudendal Nerve

↓

Relaxation of External sphincter

↓

voiding of urine

→ During micturition, flow of urine is facilitated by ↑se in abdominal pr. due to voulantary contraction of abdominal muscles.

OPPO A53
2022/07/15

→ Once micturition reflex begins, it is self-regenerative

↓

initial contraction of bladder further activates the receptors

↓

cause further ↑se in sensory impulses

↓

this in turn causes further ↑se in reflex contraction of bladder

↓

cycle continues repeatedly

↓

force of contraction of bladder reaches max^m^

↓

urine is voided out completely

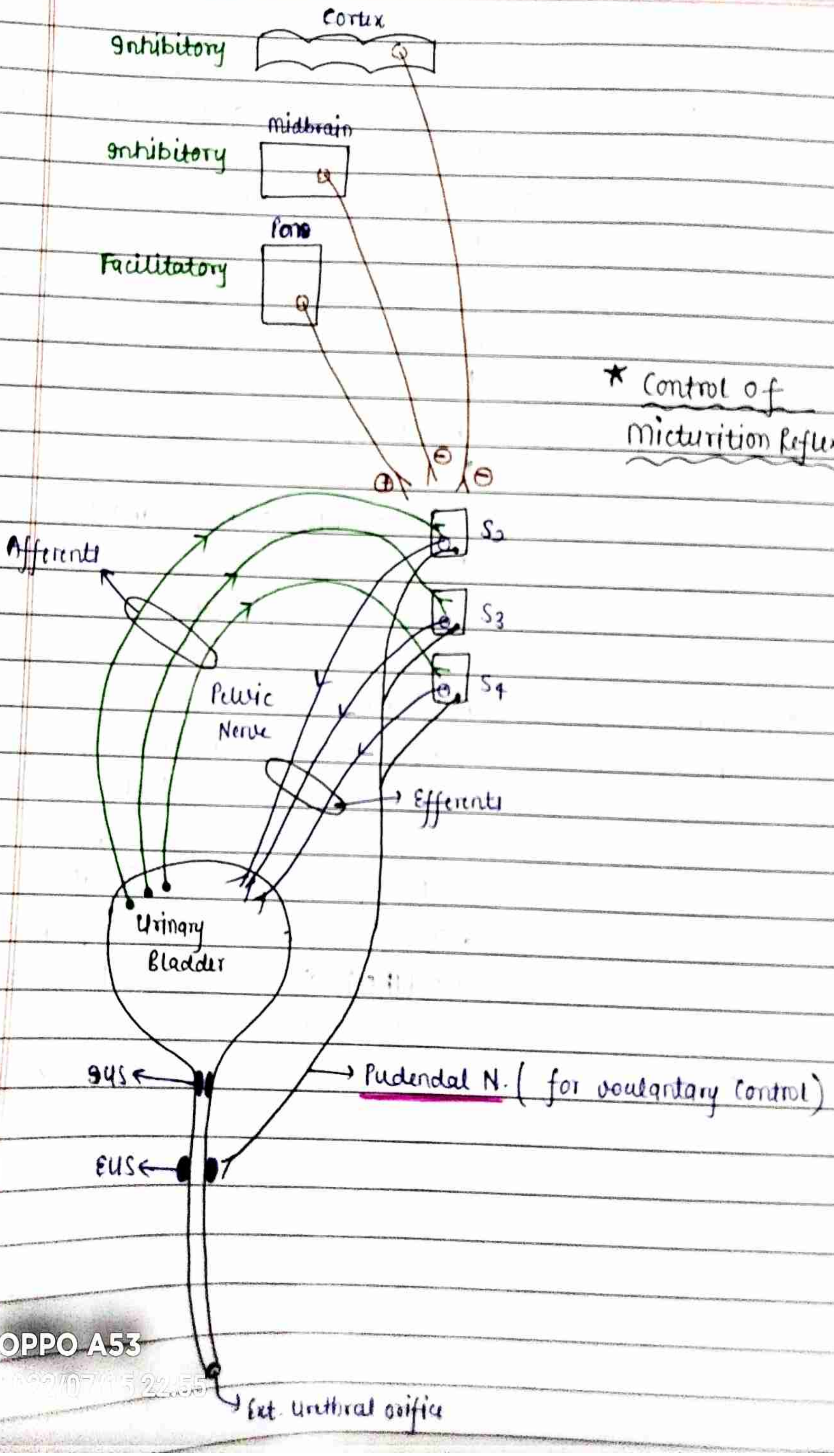
- Higher centers for Micturition

→ Spinal centers ⊕nt in ⟶ • sacral & lumbar segments
• regulated by higher centers

Inhibitory centers :	facilitatory centers
• centers in :-	• centers in :-
1. Midbrain	1. Pons
2. Cerebral Cortex	2. Some in cerebral cortex

OPPO A53
2022/07/15 22:55

★ Control of Micturition Reflex


Cortex
Inhibitory
⊖
Midbrain
Inhibitory
⊖
Pons
Facilitatory
⊕
⊕
⊖
⊖
S2
S3
S4
Afferents
Pelvic Nerve
Efferents
Urinary Bladder
IUS
EUS
Pudendal N. (for voulantary control)
Ext. Urethral orifice

⑧ FUNCTIONS of SKIN

a) Protective Function

→ Forms covering of all organs & protect organs from
- i) Bacteria & Toxic Sub.
- ii) Mechanical Blow
- iii) UV rays

i) From Bacteria & Toxic Substances

Lysozyme → • secreted in skin & destroy the bacteria

Keratinized stratum corneum → • responsible for protective functions
• offers resistance against toxic chemicals
• during injury keratinocytes secretes
↓
Cytokines → like Interleukins, α-tumor necrosis factor & γ-interferons
↓
plays imp. role in inflammation, immunological rxn, tissue repair & wound healing.

ii) From Mechanical Blow

→ Skin is somewhat loose & moves over underlying subcutaneous tissue. So, mechanical impact of any blow is not transmitted to underlying tissues.

iii) From UV-rays

→ Exposure to UV rays ↑ses production of melanin in skin
↓
melanin absorbs UV-rays

→ Stratum corneum → also absorbs UV-rays

OPPO A53
2022/07/15 22:55

2. Sensory functions

→ Considered as largest sense organ in body
→ Have nerve endings, forms specialised cutaneous receptors
↓
stimulated by sensation of touch, pain, pr., temp.
↓
convey these sensation to brain via afferent N
↓
at brain, perception of diffⁿ sensation occurs

3. Storage functions

→ Stores fat, chloride & sugar.

4. Synthetic functions

→ Vit D is synthesised in skin by action of UV-rays on cholesterol.

5. Regulation of Body Temperature

→ Excess heat is lost from body through skin by Radiation, Coduction, Convection & Evaporation.
→ Sweat Gland → Help in heat loss by secreting sweat.
→ Lipid of sebum → prevents heat loss in cold environment

6. Regulation of water & electrolyte Balance

→ Regulates by excreting water & salt through sweat.

7. Excretory function

→ Excretes small amount of urea, salts & fatty acids.

8. Absorptive functions

→ Absorb fat soluble sub & some ointments.

OPPO A53
2022/07/1 55

9. Secretory functions

→ Sweat ——→ through Sweat glands

→ Sebum ——→ —"— sebaceous glands

→ Sweat regulates body temp. & water balance

→ Sebum keeps skin moist & smooth.

⑨ BODY TEMPERATURE

* REGULATION OF BODY TEMPERATURE

→ Regulated by Hypothalamus
↓
Has 2 centres for regulation

i) Heat loss Center

→ Situated in pre-optic nucleus of Hypothalamus.
↓

→

- Neurons are heat sensitive → c/d Thermoreceptors
- Stimulation causes vasodilation & sweating
- Removal/ lesion → ↑se body temp.

ii) Heat Gain centre / Heat Production Center

→ Situated in post. Hyothalamic nucleus
↓

- Stimulation causes shivering
- Removal/ lesion → leads to fall in body temp.

Imp.

** Mechanism of Temperature Regulation

1. When body temperature ↑se

OPPO A53
2022/07/1 55

When body temp. ↑ses
↓
blood temp. ↑ses
↓
blood passes through hypothalamus
↓
stimulate heat loss center
↓
brings temp back to nrml by
- Promotion of Heat loss
- Prevention of Heat Production

a) Promotion of Heat loss → · By ↑sing secretion of sweat
· By inhibiting sympathetic center in post. hypothalamus.
↓
causes $\overset{\text{cutaneous}}{\wedge}$ vasodilation
↓
blood flow through skin ↑ses
↓
sweating ↑ses, heat loss ↑ses
↓
leads to ↓se in body temp.

b) Prevention of Heat Production → By inhibiting shivering & chemical reactions.

2. When body temp. ↓ses
→ Borught back to nrml by :- · Prevention of Heat loss
· Promotion of Heat production

OPPO A53
2022/07/15 22:55

a) Prevention of Heat loss

Body temp. ↓ses
↓
Sympathetic center in post. hypothalamus stimulates
↓
causes vasoconstriction
↓
blood flow through to skin ↓ses
↓
Heat loss ↓ses / prevented.

b) Promotion of Heat Production

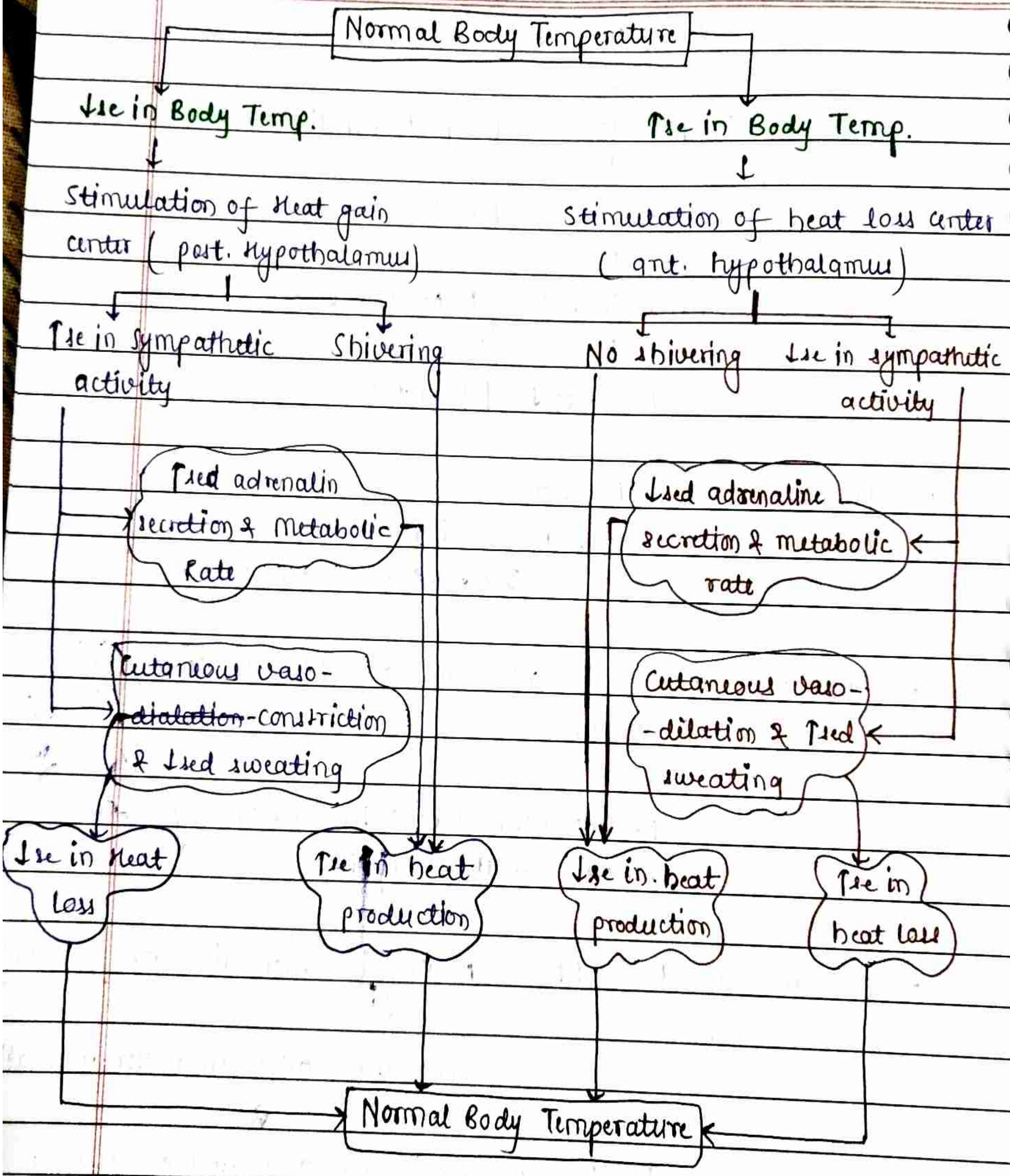
Promoted in 2 ways :- 1. Shivering
2. Increased metabolic reactions

- Shivering → • Heat gain center stimulates 1° motor center for shivering.
↓
produce enormous heat by ~~accelerating cellular~~ severe muscullar activity.

- Increased metabolic Rx^n → Heat gain center stimulates sympathetic center
↓
stimulates adrenalin & Nor-adrenalin
↓
↑ses heat production by accelerating cellular metabolic activities

② Hypothalamus secretes TRH
↓
causes release of TSH
↓
causes release of Thyroxine → ↑ses metabolic activity & heat production

OPPO A53
2022/07/15 22:56


Normal Body Temperature
↓se in Body Temp.
↑se in Body Temp.
Stimulation of Heat gain center (post. Hypothalamus)
Stimulation of heat loss center (ant. hypothalamus)
↑se in sympathetic activity
Shivering
No shivering
↓se in sympathetic activity
↑sed adrenalin secretion & Metabolic Rate
↓sed adrenaline secretion & metabolic rate
Cutaneous vaso-~~dialation~~-constriction & ↓sed sweating
Cutaneous vaso--dilation & ↑sed sweating
↓se in Heat Loss
↑se in heat production
↓se in. heat production
↑se in heat loss
Normal Body Temperature

OPPO A53
2022/07/[illegible]

ENDOCRINOLOGY

① MECHANIS OF HORMONAL ACTION

→ Does not act on target cell directly.
→ Combines with receptor to form Hormone-receptor complex.
→ This complex executes hormonal action by any 1 mechanisms:-

1. By altering permeability of cell membrane
2. By activating intracellular enzyme
3. By acting on genes

1. By altering Permeability of cell membrane

→ Neurotransmitters in synapse ⟶ acts by changing permeability of post synaptic membrane.

Ex:- In neuromuscular junction

↓

~~Axon reaches the~~

Impulse reaches the axon terminal of motor neuron

↓

Acetylcholine is released from vesicle

↓

it ↑ses permeability of post-synaptic membrane for Na

↓

By opening ligand-gated Na-channel

↓

Na^+ enters NM-junction from ECF

↓

Cause development of END plate potential

OPPO A53
2022/07/15 22:56

Date
Page

- **By Activating Intracellular Enzymes**

Protein Hr. & Catecholamines acts by this mechanism

- 1st messenger/ → • Hr. which acts on target cell
chemical mediator • Combines with receptor & forms Hr- Receptor Complex

- 2nd messenger/ → • Hr- Receptor Complex activates enzymes
Intracellular Hormonal Mediator
↓
Cause formation of 2° messenger/ Intracellular Hormonal mediator

↓

★ Most Common 2nd messenger is cyclic AMP.

Others :- 1. Calcium ion & Calmodulin → activates Myosin Kinase

2. Inositol Triphosphate (IP_3) & Diacylglycerol → activates Phospholipase C via G-Protein

3. Cyclic GMP
- acts same as CAMP
- activates Protein kinase

Imp. ★★ Cyclic AMP

→ Cyclic AMP/ CAMP/ Cyclic adenosine 3'5'- monophosphate

→ Acts as 2° messenger for Protein Hr. & Catecholamines

★ Formn of cyclic AMP → Role of G-Protein

→ G-protein/ Guanosine Nucleotide - Binding Protein
↓
- membrane proteins
- Situated on inner surface of cell mem.
- Plays imp. role in formn of cAMP.
- Made up of trimeric subunit c/d α, β & γ.
- α → responsible for biological actions
  - ↘ Binds with GDP & forms α - GDP unit
  - ↙ Have intrinsic enzyme activity c/d GTPase activity

- β & γ always binds together to form β-γ dimer.
- In inactivated state, α-GDP & β-γ dimer ⇒ united

* Sequence of Events in formn of cAMP

Hormone binds with receptor in cell membrane

↓

forms Hr- receptor complex

↓

Activates G-protein

↓

Protein release GDP from α-GDP unit

↓

α-subunits binds with new molecule of GTP i.e., GDP exchaned for GTP

↓

Exchange triggers the dissociation of α-GTP & β-γ dimer from receptor

↓

Now, α-GTP & β-γ dimer activates the 2nd messenger pathway

↓

α-GTP unit activates the adenyl cyclase

↓

Activated adenyl cyclase converts adenosine triphosphate (ATP) in cytoplasm to cAMP.

↓

cAMP executes action of Hr. and activate the enzyme like protein kinase A

↓

cAMP Produces response depending upon function of Target cell through this enzyme.

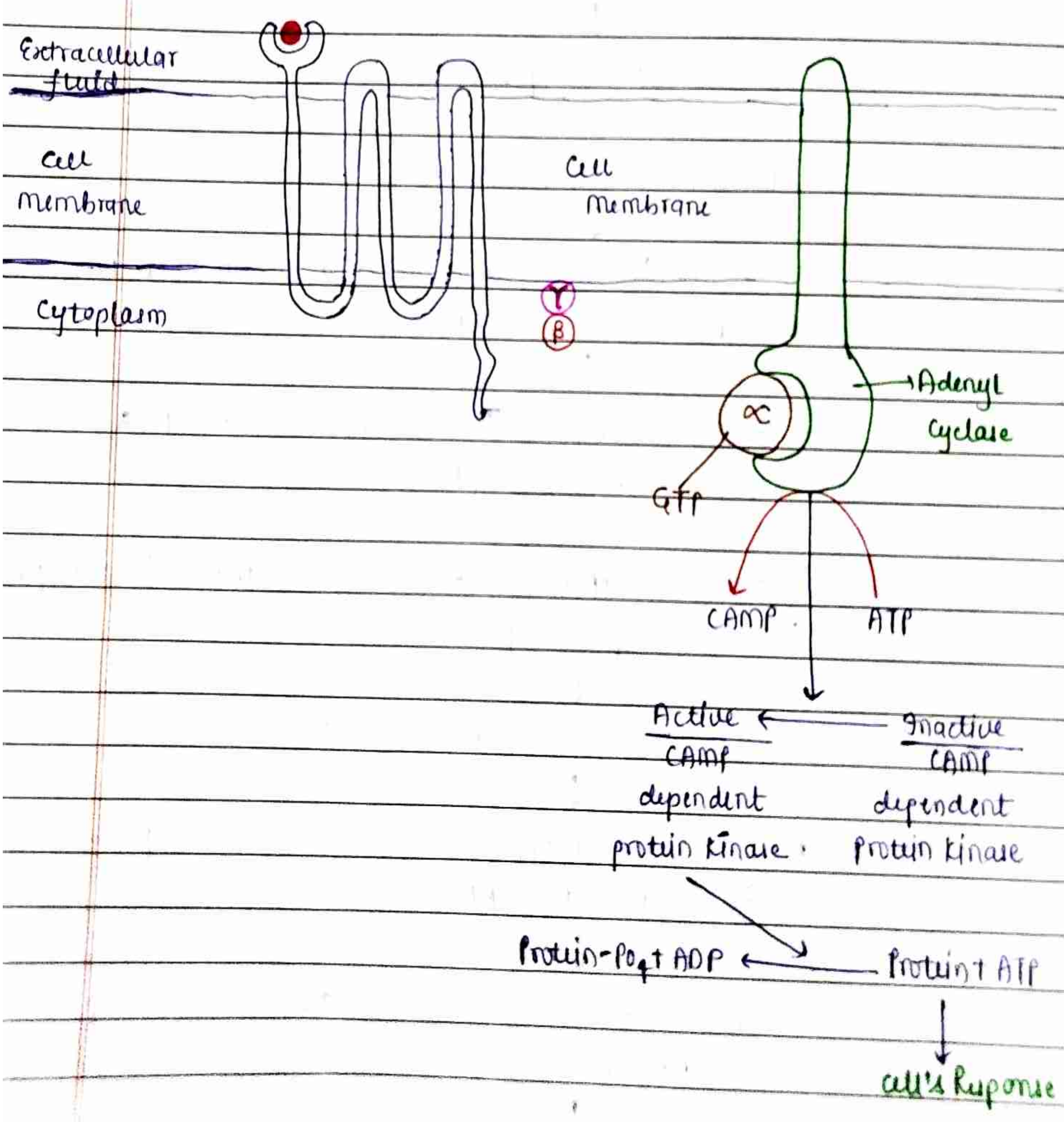
OPPO A53
2022/07/15 22:56

OPPO A55
2022/07/15 22:56

Date ______
Page ______

Responses produced by CAMP

1. Contraction & Relaxation of muscle
2. Alternation in permeability of cell mem.
3. Synthesis of sub. inside cell
4. Secretion or Release of sub by cell
5. Can control other physiological activities also.


Extracellular fluid
cell membrane
Cytoplasm
Cell membrane
γ
β
α
Adenyl cyclase
GTP
CAMP
ATP
Active CAMP dependent protein kinase
Inactive CAMP dependent protein kinase
Protein-PO4 + ADP
Protein + ATP
cell's Response

OPPO A53
2022/07/15 22:56

Date
Page

*** Inositol Triphosphate & Diacylglycerol**

Hr. + Receptor ⟶ Hr- Receptor Complex

↓

G- Protein

↓

Phospholipase-C

↓ converts

Phosphatidylinositol biphosphate (PIP_2)

↓ into

IP_3 + Diacylglycerol

↙ ↓ activates

diffuses into Endoplasmic Reticulum | Protein kinase C

↓

Produce physiological action by releasing Ca.

3. **By Acting on Genes**

Thyroid & Steroid Hr. execute their function by acting on genes in target cell.

*** Sequence of Events**

Hr. Enters interior of cell

↓

Binds with receptor in cytoplasm

↓

forms Hr-Receptor complex

↓

Complex binds with DNA & ↑se transcription of m-RNA

↓

Date ______
Page ______

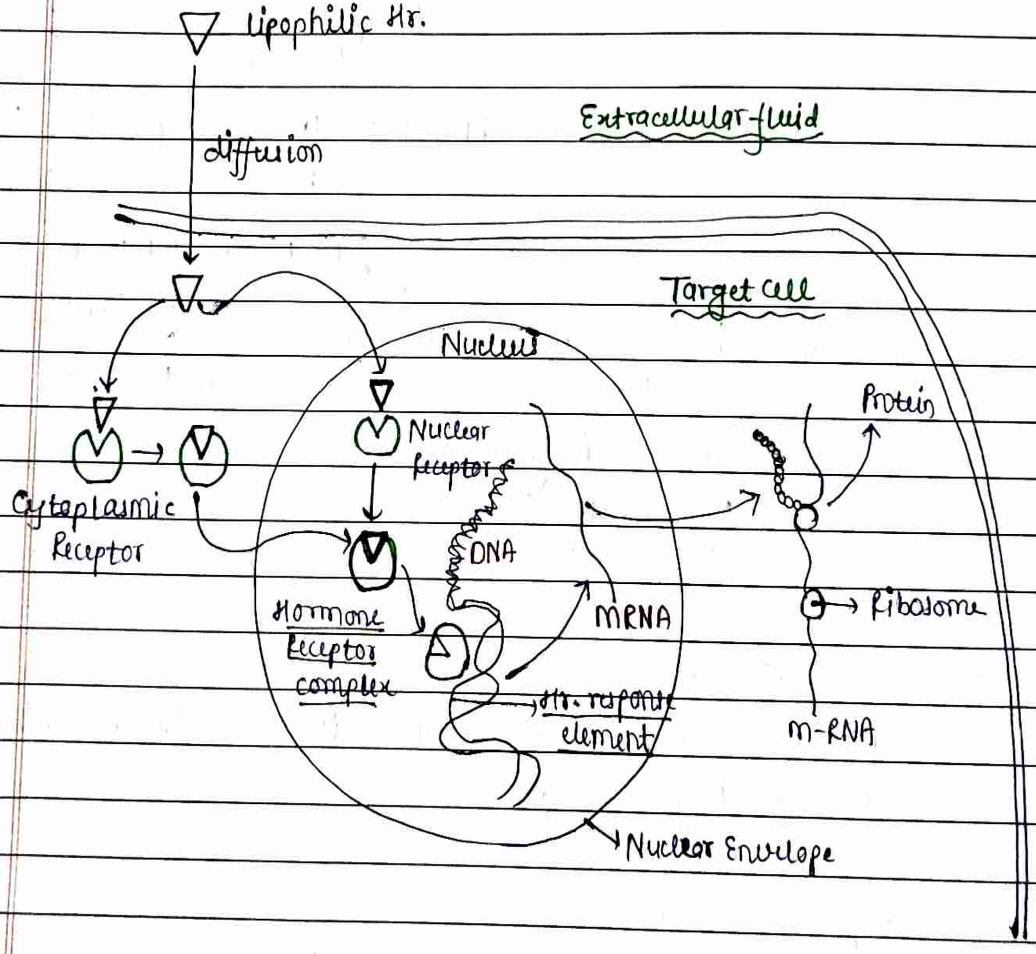
mRNA moves out of nucleus & activates ribosomes

↓

Ribosome produces large quantity of protein

↓

Protein produces physiological responses in target cell


Lipophilic Hr.
diffusion
Extracellular fluid
Target cell
Nucleus
Nuclear Receptor
Cytoplasmic Receptor
DNA
Hormone Receptor complex
MRNA
Hr. response element
Protein
Ribosome
m-RNA
Nuclear Envelope

OPPO A53
2022/07/15 22:56

OPPO A53
2022/07/15 22:56

Date ____
Page ____

②;

PITUITARY GLAND

★ Development of Pituitary Gland

Ant. Pituitary → · Ectodermal in origin
· Arises from pharyngeal epithelium as upward growth of Rathke Pouch.

Post. Pituitary → · Neuro-Ectodermal in origin
· Arises from Hypothalamus as downward diverticulum.

★ Hormones Secreted by Anterior Pituitary
1. Growth Hr. / Somatotropic Hr. (STH)
2. Thyroid Stimulating Hr. (TSH) / Thyrotropic Hr.
3. Adrenocortico-tropic Hr. (ACTH)
4. Follicle Stimulating Hr. (FSH)
5. Gonadotrophich Hr. (GH) → FSH in female, LH in male
6. Prolactin (PRL)

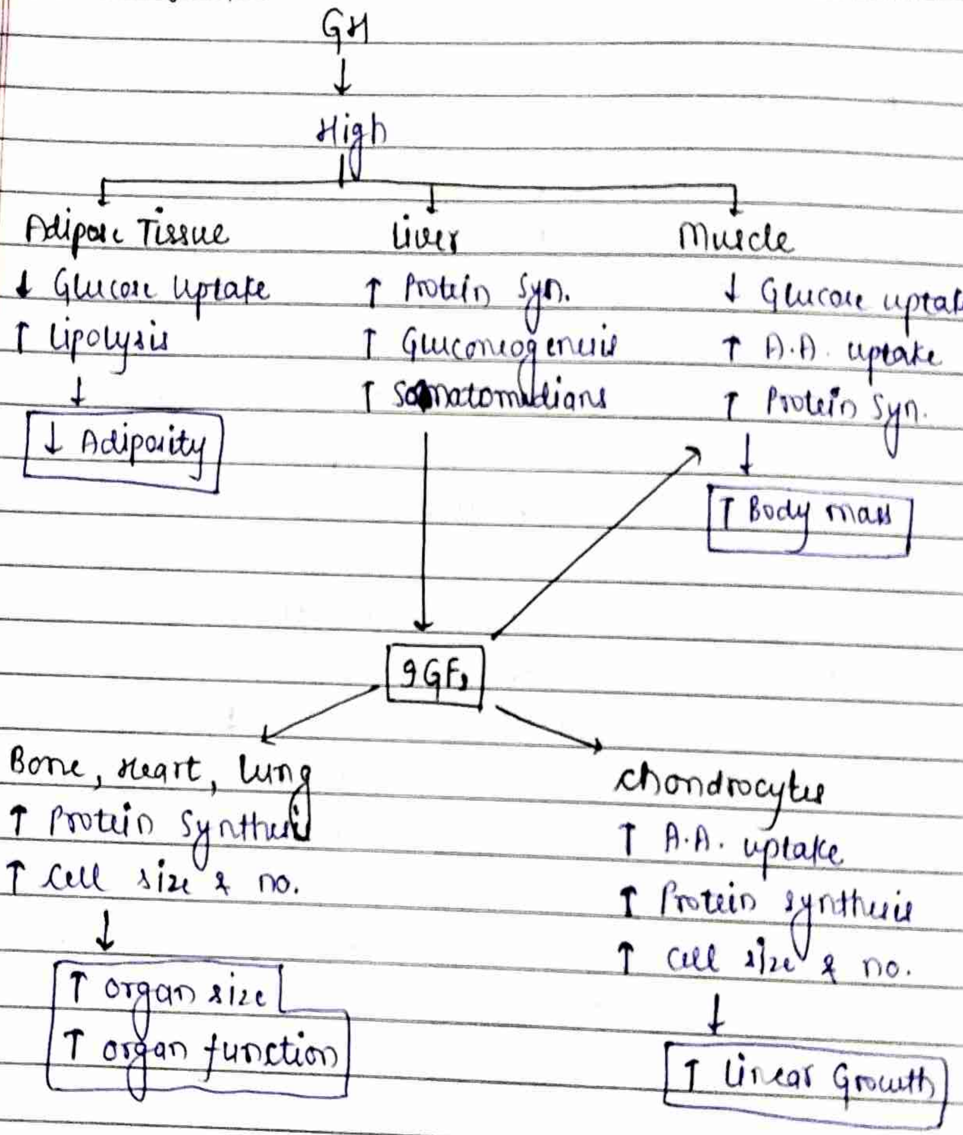
→ GROWTH HORMONE
- Secreted by Somatotrophs → acidophillic cells of Ant. Pituitary
- Protein in nature

Transport → Transported in blood by GH-Binding Proteins (GHBPs).

Half life & Metabolism → · HL = 20 min
· Degraded in liver & Kidney.

OPPO A53
2022/07/15 22:56

* Actions of GH


GH
High
Adipose Tissue
↓ Glucose uptake
↑ Lipolysis
↓ Adiposity
Liver
↑ Protein Syn.
↑ Gluconeogenesis
↑ Somatomedians
Muscle
↓ Glucose uptake
↑ A.A. uptake
↑ Protein Syn.
↑ Body mass
IGFs
Bone, heart, lung
↑ Protein Synthesis
↑ cell size & no.
↑ organ size
↑ organ function
chondrocytes
↑ A.A. uptake
↑ Protein synthesis
↑ cell size & no.
↑ Linear Growth

OPPO A53
2022/07/15 22:56

Date
Page

★ Mode of Action → Somatomedin

→ GH acts on bones, growth & protein metabolism through Somatomedin → secreted by liver.

→ GH stimulates liver to secrete somatomedin

→ Sometimes, in spite of nrml secretion of GH
↓
Growth is arrested (dwarfism)
↓
due to absence / defeciency of Somatomedin

→ Somatomedins are of 2 types

- Insulin-like growth factor - I (IGF-I) $\xrightarrow{\text{called}}$ Somatomedin-C
- Insulin-like growth factor - II

Somatomedin C → acts on bones & protein metabolism

Insulin like growth factor II → role in growth of foetus

★ Regulation of Secretion

Hypothalamus & Feedback mechanism regulates secretion of GH

GH secretion stimulated by →
- Hypoglycemia
- Fasting
- Starvation
- Exercise
- Stress & Trauma
- Initial stage of sleep

GH secretion inhibited by →
- Hyperglycemia
- ↑se free fatty acids in blood
- Later stage of sleep

OPPO A53
2022/07/15 22:56

★ Role of Hypothalamus

→ Regulates via 3 Hormones

1. Growth Hr. Releasing Hr. (GHRH) → ↑ses GH secretion by stimulating the somatotrophs of Ant. pituitary

2. Growth Hr. Releasing Polypeptide (GHRP) → ↑ses GHRH from Hypothalamus & GH from pituitary

3. Growth Hr. - Inhibitory Hr. (GHIH) / Somatostatin → ↓ses GH secretion, also secreted by δ-cells of pancreas.

★ Feedback Control

→ under -ve feedbak control

→ Hypothalamus releases GHRH & GHRP

↓

Promotes release of GH from pituitary

↓

GH acts on various tissues :

Activates liver to release Somatomedin C (IGF-1)

↓

IGF-1 ↑se release of GHIH from hypo.

↓

GHIH inhibits release of GH

→ Somatomedin also inhibits release of GHRP

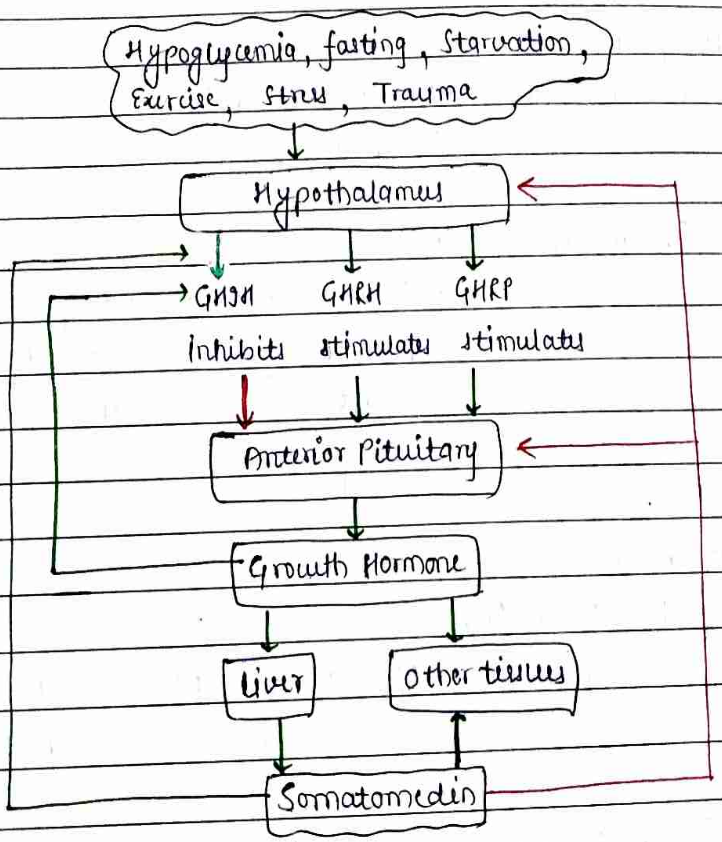
→ Acts directly on pituitary & inhibits release of GH.

→ GH inhibits ~~on~~ its own secretion by stimulating release of GHIH, this feedback is c/d short-loop feedback.

Date ______
Page ______

* Role of Ghrelin in secretion of GH

- Ghrelin is peptide Hr. → • synthesised by epithelial cells in fundus of stomach.
- Also produce in Hypothalamus, pituitary, kidney, Placenta (in small amount)
- Promotes secretion of GH by stimulating somatotrophs.


Hypoglycemia, fasting, Starvation, Exercise, Stress, Trauma
Hypothalamus
GHIH
GHRH
GHRP
Inhibits
stimulates
stimulates
Anterior Pituitary
Growth Hormone
Liver
Other tissues
Somatomedin

* Regulation of GH Secretion

Red line → Inhibition

Green line → Stimulation

OPPO A53
2022/07/15 22:56

OPPO A53
2022/07/15 22:56

→ Thyroid Stimulating Hr. (TSH)
- Necessary for growth & secretory activity of thyroid gland.

→ Adrenocorticotrophic Hr. (ACTH)
- Necessary for structural integrity & secretory activity of adrenal cortex.

→ Follicle Stimulating Hr. (FSH)
- Glycoprotein in nature.

Functions in males :- • Along with testosterone stimulates process of spermatogenesis.

Functions in females :-
- Causes development of grafian follicle
- Causes secretion of estrogen
- Promotes aromatase activity in granulosa cells & cause conversion of androgen into estrogen.

→ Luteinizing Hr. (LH)
- Glycoprotein in nature

Functions in males :- • K/n as ICSH b/c stimulates interstitial cells for secretion of Testosterone.

Functions in females :-
- Responsible for ovulation
- Imp. for formn of corpus luteum
- Activates secretory functions of corpus lu

→ Prolactin (PRL)
- Single chain polypeptide Hr.
- Necessary for final preparation of mammary gland for production & secretion of **Milk**.
- Acts directly on epithelial cells of mammary gland & causes Alveolar Hyperplasia.

OPPO A53
2022/07 5 22:57

★ Hormones Secreted by Posterior Pituitary

1. ADH / Vasopressin (AVP)] are c/d Neurohormones
2. Oxytocin

→ ANTIDIURETIC HORMONE (ADH)

- Source of Secretion → • Secreted mainly by **Supraoptic nuclei** of hypothalamus.

  from here transported to post. pituitary through nerve fibres of hypothalamo - hypophyseal tract, by axonic flow

- Actions → Retention of water
  Vasopressin Action

a) Retention of Water

→ **Major function of ADH**

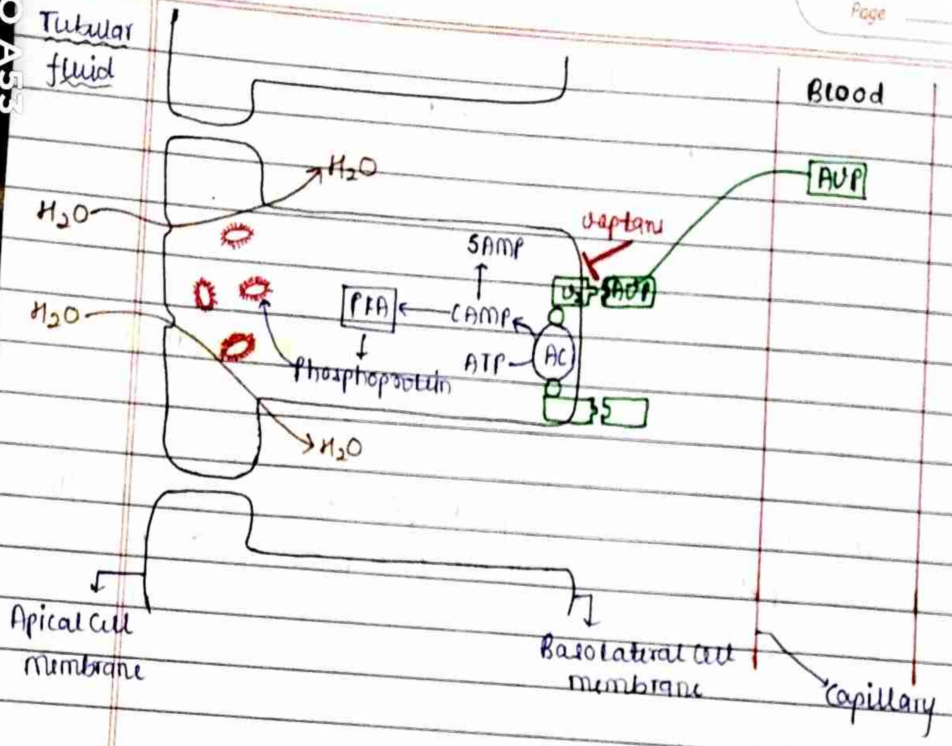
→ Increases facultative reabsorption of water from DCT & CD.

In absence of ADH :- • DCT & CD → totally impermeable for H_2O

- Reabsorption of water does not occurs & leads to loss of large amount of water.
- Condn is c/d **Diabetes Incipidus** & excretion of large amount of water is c/d Diuresis.

→ Ise water reabsorption by regulating the water protein channels c/d Aquaporins through V_2 - receptors.

Osmoreceptors → ⊕nt in hypothalamus & cause release of ADH in response to change in osmotal conc. of blood.


Tubular fluid
H₂O
H₂O
H₂O
H₂O
Blood
AVP
vaptans
V2
ADH
5AMP
cAMP
PKA
ATP
AC
Phosphoprotein
Apical cell membrane
Basolateral cell membrane
Capillary

Cellular Action of AVP/ADH on collecting Duct cells
[Principal cells]

b) Vasopressin Action

→ Minute conc. of ADH → caused ↑ed conservation of H_2O by kidney
→ Higher conc. of ADH → Have potent effect of constricting arteriole.

↓

thus ↑sing arterial pressure

↓

for this reason ADH is c/d Vasopressin

** Regulation of Secretion → Stimulants for secretion are :-
→ ↓se in extracellular fluid (ECF) vol.

OPPO A53
2022/07/15 22:57

→ OXYTOCIN

- Source of Secretion → • Secreted mainly by paraventricular nucleus of hypothalamus.
- Secreted in both males as well as females

- Action in females
  1. Acts on mammary gland
  2. Acts on uterus

1. Action of oxytocin on mammary gland

→ Causes ejection of milk

→ Glands are lined by myoepithelial cells

↓

Causes contraction of these cells & flow of milk from alveoli

↓

to exterior through duct system & nipple

↓

This whole process is c/d **Milk Ejection Reflex** / Milk letdown Reflex (Neuroendocrine reflex)

** Milk Ejection Reflex

Plenty of touch receptors ⊕nt on gland, particularly near nipple

↓

when infant suckles mother nipple

↓

Touch receptors are stimulated

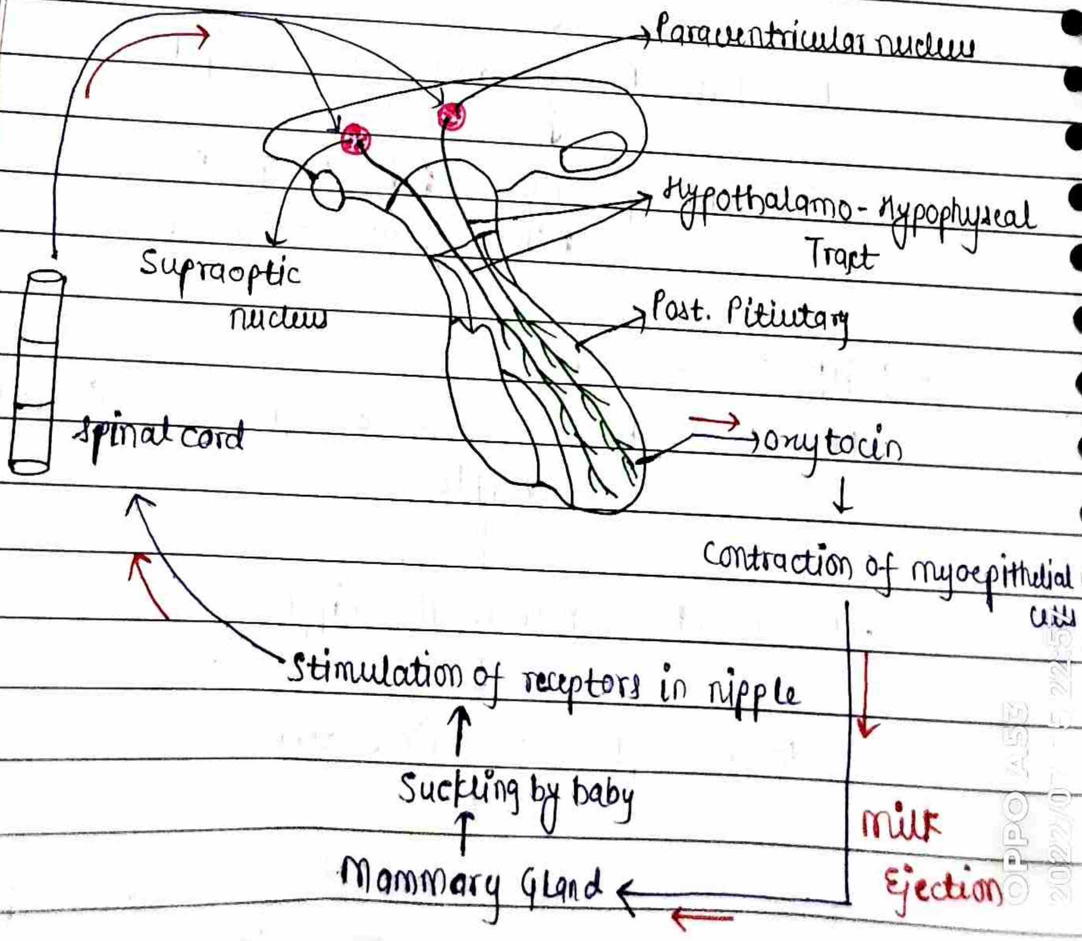
↓

Impulse via somatic efferent fibres carried to paraventricular & supraoptic nuclei

Hypothalamus send impulse to post. pituitary
↓
Efferent impulses causes release of oxytocin into blood
↓
oxytocin reaches mamary gland & causes contraction of myoepithelial cells
↓
Results in ejection of milk

→ As, Reflex is initiated by Nervous factor completed by Hormonal Actions.
↓
So, c/d Neuro-endocrine Reflex

→ During reflex, large amount of oxytocin released by ⊕ve feedback mechanism.


Paraventricular nucleus
Hypothalamo-Hypophyseal Tract
Supraoptic nucleus
Post. Pituitary
spinal cord
oxytocin
Contraction of myoepithelial cells
Stimulation of receptors in nipple
Suckling by baby
Mammary Gland
Milk Ejection

OPPO A53
2022/07/15 22:5

2. **Action of oxytocin on Males**
- → Release Tses during ejaculation.
- → facilitates release of sperm into urethra → by contraction of smooth muscles in reproductive tract.

** Mode of Action of oxytocin

Acts on mammary gland & uterus by activating G-protein coupled oxytocin receptors.

DISORDERS OF PITUITARY GLAND
[ANTERIOR PITUITARY]

1. **Gigantism**

→ Charactrised by excess growth of body / long bones results in abnormal height (7-8 feet) with huge status.

Causes :- • Hypersecretion of GH in childhood or in preadult before fusion of epiphysis of long bones with shaft.
• Hypersecretion occurs b/c of tumor of acidophillic cells in ant. pituitary

Signs & Symptoms :-
1. Large hands & feet
2. Giants are hyperglycemic & develop glycosuria & pituitary diabetes.
3. Hyperglycemia causes constant stimulation of β-cells of pancreas → overactivity of β-cells leads to degeneration of these cells → ultimately Diabetes mellitus due to defeciency of Insulin.
4. Tumor of pituitary causes const. Headache
5. Tumor also causes visual disturbances.

OPPO A53
2022/07/15 22:57

OPPO A53
2022/07/15 22:57

Imp# 2. ACROMEGALY

→ characterised by enlargement ~~of~~, thickening & broadening of bones, particularly in extremities of body.

Causes :- • Hypersecretion of GH in adults after fusion of epiphysis with shaft.

• Hypersecretion occurs due to tumor of acidophillic cells in ant. pituitary.

Signs & Symptoms :-

1. Acromegalic / Gorilla face → face with rough features
   - Protrusion of Supraorbital ridges
   - Broadnening of Nose
   - Thickened lips
   - Wrinkled forehead
   - Prognathism → protrusion of lower jaw

2. Enlargement of hands & feet

3. Kyphosis → extreme curvature of upper back

4. Thickening of scalp & wrinkles on scalp (bulldog scalp)

5. Overgrowth of body hairs

6. Hyperactivity of Thyroid, Parathyroid & Adrenal

7. Hyperglycamia & glucosuria results in DM.

8. Hypertension, Headache & Visual disturbance (Bitemporal Heminopia)

OPPO A53
2022/07/15 22:57

Imp.

DWARFISM (Pituitary disorder in children)

→ characterised by stunted growth

- Causes :- • Hyposecretion of GH in infancy / early childhood
  - Occurs b/c of following reasons :-
  1. Tumour of chromophobes → most common cause
  2. Deficiency of Somatomedin-C
  3. Atrophy / Degeneration of acidophillic cells in Ant. pituitary
  4. Panhypopituitarism → Reduction in secretion of all Hr. of ant. pituitary

- Signs & Symptoms :-

1. Stunted Skeletal growth → maxm ht. of adult age is only 3 feet.

2. proportions of diffn parts of body are nrml, only head becomes slightly larger

3. Mental activity is nrml with no mental retardation

4. Reproductive functions → nrml if there is only GH deficiency
   In panhypopituitarism, dwarf do not attain puberty due to lack of gonadotropins.

★ **African Pygmy & Levi Lorain Dwarf**

Rate of GH secretion is Normal / High but there is heredita
inability to form Somatomedin C, which is a key step
for promotion of growth by GH.

Date
Page

[POSTERIOR PITUITARY]

1. Syndrome of Inappropriate Hypersecretion of ADH [SIADH]

→ Characterized by loss of sodium through urine due to hypersecretion of ADH.

→ Effects of ADH excess are seen despite of Hypo-osmolality :-

1. Water Retention
2. Hypernatriuria
3. Hyponatraemia
4. Oedema

Imp. 2. DIABETES INSIPIDUS

→ Characterised by excess excretion of water through urine.

* Central DI → failure to produce ADH

↓

• Occurs due to deficiency of ADH, due to following

Causes :- reasons :- 1. Lesion of Supraoptic & paraventricular nuclei.
2. Lesion in hypothalamo-hypophyseal tract
3. Atrophy of Post. Pituitary

Signs & Symptoms :-

1. **Polyuria** → Excretion of large quantity of dilute urine, with ↑sed frequency of voiding.

2. **Polydipsia** → Intake of excess of water
B/c of polyuria → water is lost from body

↓

stimulates thirst center in hypothalamus

↓

Results in intake of large quantity of water

OPPO A53
2022/07/15 22:57

3. **Dehydration** → • In some cases, thirst center is also affected due to lesion.

↓

so, water intake ↓ses and

↓

~~but~~ loss of water is not compensated

↓

so, Dehydration develops

★ Nephrogenic DI → Inability of kidney to respond to ADH

↓

- genetic disorder caused by mutation of genes of V_2 receptor / Aquaporins 2.
- Treated by treating underlying renal disease.

★★ Central DI can be treated by administring a synthet analog of ADH, DESMOPRESSIN (DDAVP), acts selectivel on V_2-receptors to ↑se water permeability in DCT & CD.

OPPO A53
2022/07/15 22:58

OPPO A53
2022/07/15 23:02

Date

① Thyroid Gland

★ Thyroid Hormones :- Principal Hormones are :-

1. T_4 (Thyroxine) → 93 %
2. T_3 (triiodothyronine) → 7 %
3. RT_3 (reverse triiodothyronine)
4. Calcitonin

→ T_3, T_4 & calcitonin → Thyroid follicles

→ calcitonin → parafollicular cells (C-cells)

→ ★ T_3 is 4 times more active then T_4.

→ T_4 is eventtually converted to T_3 in tissue, T_4 is mainly a prohormone.

→ RT_3 → inactive.

★ Steps in the Biosynthesis of Thyroid Hr.

1. Iodine trapping
2. Oxidation of idodide ion
3. Organification of thyroglobulin
4. Coupling of iodotyrosine residues.
5. Release of T_3 & T_4 into blood.

1. Iodine Trapping

→ Transport of iodide from blood into thyroid glandular cells.

↓ is achived

Pumping of iodide, by the action of Sodium-Iodine Symporter, cotransports 1 I^- along with 2 Na^+ in thyroid follicular cells.

↓

#

Thyroid Hr. are synthesised in thyroglobulin
↓
remain bound to it till they are secreted.

- → Energy is achieved by Na^+-K^+ Atpase pump (help to establish low intracellular Na^+ conc.
- → Rate is influenced by TSH.
- → PENDRIN → protein help iodide transport out of thyroid cells into follicle.

2. Oxidation of Iodide into Iodine
- → Iodide is immediately converted into Iodine by oxin.
- → $I^- \rightarrow I$ (k/n as organification)
- → facilitated by enzyme thyroid peroxidase.

3. Thyroglobulin Synthesis →
- •occurs in ER of thyroid cells
- •secreted into colloids by exocytosis
- •facilitated by thyroid peroxidase.

- → Binding of I with the thyroglobulin molecule is c/d organification (iodination of Tyrosine)
- → facilitated by tyrosine peroxidase.
- → Tyrosine ⟶ monoiodotyrosine ⟶ di-iodotyrosine

4. Coupling Rxn
- → Mono & di-iodo. → coupled with each other.
- → T_4 = 2 di-iodo. , T_3 = mono. + di-iodo.
- → Each thyroglobulin molecule contains → 30 T_4 & few T_3.
- → Stores for atleast supply for 2-3 months.
- → when synthesis ceased, effects of deficiency not observed for several months.

OPPO A53
2022/07/15 23:02

Date

5. Release of T_3 & T_4 & Proteolysis of Thyroglobulin

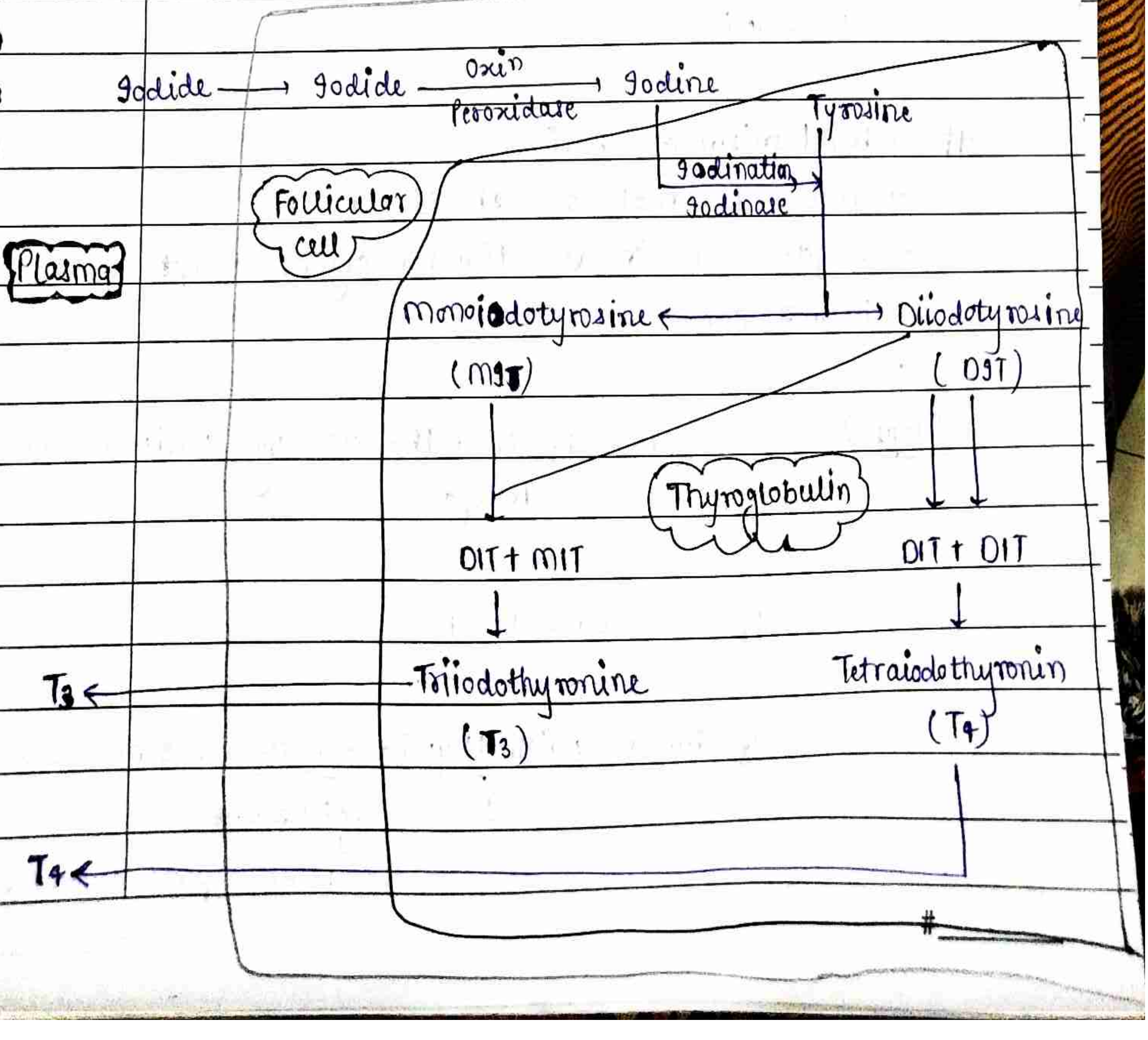
→ Thyroid ingest colloids by Endocytosis.

→ lysosomal enzymes → causes proteolysis of thyroglobulin molecule → forms T_3, T_4, MIT & DIT

*not secreted by gland

T_3, T_4 → released into general circulation

MIT & DIT → deiodinated by iodotyrosine deiodinase
↓
iodine released is used by the gland for further synthesis of Hr.
↓
this supplies more I in comparison to pump.


Iodide
Iodide
Oxin
Peroxidase
Iodine
Tyrosine
Iodination
Iodinase
Follicular cell
Plasma
Monoiodotyrosine
(MIT)
Diiodotyrosine
(DIT)
Thyroglobulin
DIT + MIT
DIT + DIT
Triiodothyronine
(T_3)
Tetraiodothyronin
(T_4)
T_3
T_4
#

OPPO A53
2022/07/15 23:02

Regulation of Secretion

Regulated by feedback control mechanism.

Hypo. secretes Thyrotropin Releasing Hr. (TRH)
↓ stimulates
Ant. pituitary to secrete TSH.
↓ stimulates
Thyroid gland to secrete T_3 & T_4.

- → There is counter regulation of TSH by thyroid Hr.
- → plasma conc. of T_3 & T_4 provides feedback signal for release of TRH & TSH.
- → plasma conc. of TSH is better index of thyroid activity
- → dopamine, somatostatin & glucocorticoid inhibits TSH secretion.

Mechanism of Action

- → Similar to that of steroid Hr.
- → Receptors ⊕nt in all tissues & organs except adult brain & gonads.

Steps :-

T_3 & T_4 enter the cell by carrier mediate transport.
↓
T_4 is converted to T_3
↓
T_3 binds with thyroid Hr. receptor ⊕ on nucleus.
↓
TRE element
↓
Thyroid Hr. response element.

OPPO A53
2022/07 23:02

Date

↓
TRF
↓
Ant Pit ←
↓
TSH
↓
Thyroid G.
↓
T_3 & T_4

Causes Transcription of DNA
↓
↑ses translation of mRNA.
↓
↑se protein synthesis that stimulates
↓
cell growth & maturation, intracellular enzyme, mito. formn, resp. enzymes synthesis, $Na^+ - K^+$ ATPase activity
↓
↑ses cellular O_2 consumption, BMR

Actions / Role in Body

→ Control Basal energy metabolism, development of CNS, nrml growth in childhood.

1. Effects on Basal metabolism

→ Hr. ↑ses basal rate of O_2 consumption
↓
↑ses basal metabolism
↓
↑ses rate of heat production
↓
c/d Calorigenic / Thermogenic Actions of Hr.

→ metabolism is also activated by $Na^+ - K^+$ ATPase activity

→ T_3 → stimulates transcription of genes for both α & β subunits of $Na^+ - K^+$ pump.

#

OPPO A53
2022/07/15 23:02

2. Effects 2° to metabolic or thermogenic action

↑se N_2 excretion

↑se metabolism, ↑se body temp.

↑se vitamins requirement

3. Effect on nervous system

Essential for development of CNS especially during infancy.

4. Effects on growth & development

→ Essential for nrml growth & musculoskeletal maturation.

→ Promote GH secretion & expression of genes of GH.

→ facilitate effect of GH on tissue.

5. Cardiovascular Effects

↑es heart rate & myocardial ~~output~~ contractility.

∴ ↑es cardiac output.

6. Effects on Intermediary metabolism

On carbo. metabolism → ↑es absorption of glucose from intestine.

On fat metabolism → ↑es lipolysis i.e., release of free fatty acids & glycerol from adipose tissue.

On protein metabolism → ↑es proteolysis in skeletal muscles.

On metabolic action of other hr. → ↑es action of catecholamines, glucagons, cortisol & GH.

* Have widespreaded effect on
metabolism, growth & development

Date ☐☐☐

7. Effects on Sympathetic Nervous System
function similar to the effect of SNS, i.e., ↑sing metabolism, heat production, heart rate & neuro-muscular functions.

8. Effects on Respiratory System
- → ↑ses O_2 utilisation of tissue.
- → Stimulates erythropoiesis by ↑sing erythropoietin secretion i.e., O_2 supply to tissue ↑ses.

9. Effects on GI Tract
- → Enhances motility of GI Tract
- → ↑se apetite & food intake.
- → Hyperthyroidism → Hyperdefecation
  Hypo —"— → Constipation

10. Effect on Skeletal muscles
- → ↑ses expression of MCH genes on Skeletal muscles.
- → Hypothy. → muscle cramp & weakness
- → Hyperthy. → Myopathy.

11. Effect on Reproductive Tract
In women → ↑ses follicular maturation & ovulation
In males → ↑ses spermatogenesis

12. Effect on Kidney
↑ses kidney size, growth of tubular cells, renal blood flow, GFR, reabsorption of electrolytes, glucose & water.

OPPO A53
2022/07/15 23:02

OPPO A53
2022/07/15 23:02

Hypothyrodism (In adult K/n as Myxedema)

★ Etiology :- acc. to cause

1°

↓

- develop due to disease or a cause that mainly effect thyroid gland.
- Common causes :-

1. Autoimmune
2. Iathrogenic → use of radioiodine
3. Iodine defeciency
4. Drugs → excess use of antithyroid drug
5. Congenital

2°

↓

- develops due to defect outside the thyroid gland, usually due to defect either in pituitary or in hypothalamus.
  - Pituitary hypothyrodism] Pit. resection, tumor, Sheehan's syndrome (Postpartum necrosis of Pituitary)
  - Hypothalamic hypo. → due to injury or tumor.

★ **Features**

1. Symptoms :- Cold intolerance, weakness, constipation, wt. gain, thick & husky voice, yellow skin.

2. Signs → Cool extremities, puffy face with edematous hand & feet (myxedema).

→ BMR ↓es to −90, plasma cholesterol ↑es.

3. Diagnosis → T_3 & T_4 ↓ses but TSH ↑ses by feedback
In hypopituitary & hypothalamic → TSH conc. ↓ses +
T_3 & T_4 also ↓ses.

4. Treatment → • Thyroid. Hr. replacement
• T_4 is given at a dose (10-15 ug/kg/day).

Cretinism (Hypo. in children)

↓

when develop before or just after birth, patients c/d Cretins.

Cause :- • Maternal Iodine deficiency
• Maldevelopment of thyroid gland.
• Inborn error of thyroid Hr. synthesis

Features :- dwarf, mentally retarted, potbelly & protrusion of tongue.

Treatment :- • prevented if diagnosed & treated immediately.
• Thyroid Hr. replacement early in infancy can totally cure.

Hyperthyrodism

① Graves Disease

→ Autoimmune disease and is most common cause of Hyperthyrodism

→ In Graves' disease, B-lymphocytes produces autoimmune

#

OPPO A53
2022/07 5 23:02

antibodies c/d Thyroid Stimulating Antibodies (TSAbs)

→ These antibodies acts like TSH by binding with mem. receptors of TSH & activating cAMP system of thyroid follicular cells, results in hypersecretion of Thyroid Hr.

→ Antibodies acts for a long time even upto 12 Hr. while TSH lasts only for an hour.

→ High conc. of thyroid Hr. caused by Antibodies supresses the TSH production.

→ So, conc. of TSH is low or almost zero, in plasma of Hyperthyroid patients.

OPPO A53
2022/07/15 23:08

④ PARATHYROID GLAND

★ HYPOPARATHYROIDISM - HYPOCALCEMIA

→ Hyposecretion of PTH = Hypoparathyroidism
↓
leads to Hypocalcemia

→ Causes

1. Surgical removal of parathyroid gland [Parathyroidectomy]
2. Removal of parathyroid gland during surgical removal of thyroid gland [Thyroidectomy]
3. Autoimmune disease
4. Defeciency of receptors of PTH in target cells.

★★ Hypocalcemia & Tetany

→ Hypoparathyroidism leads to hypocalcemia
↓
by decreasing resorption of calcium from bones

→ Hypocalcemia causes → Neuromuscular hyperexcitability
↓
results in Hypocalcemic Tetany

→ Tetany occurs when plasma Ca^{++} level falls below 6 mg/dL from its normly value of 9.4 mg/dL

★ TETANY

→ Abnorml cond^n characterized by violent & painful muscular spasm [spasm = involuntary muscular contraction], particularly in feet & Hand.

↓

b/c of Hyperexcitability of nerves & skeletal muscles due to Ca^{++} deficiency

★ Signs & Symptoms

① Hyperreflexia & Convulsions

→ Increase in neural excitability $\xrightarrow{\text{causes}}$ Hyperreflexia

↓ causes ↓ (overactive reflex action)

→ convulsive muscular contraction

② Carpopedal Spasm

→ Spasm in Hand & feet → occurs in Hypocalcemic tetany

→ During spasm hand shows

↓

- flexion at wrist joint
- Flexion at metacarpophalangeal joint
- Extension at interphalangeal joint
- Adduction of thumb

③ Laryngeal stridor

→ Stridor means noisy breathing

→ laryngeal stridor → • loud crowing sound during inspiration
• occurs due to **Laryngospasm** (involuntary contraction of laryngeal muscles).

④ Cardiovascular changes

→ Dialation of Heart

→ Arrhythmias

→ Hypotension

→ Heart failure

OPPO A53
2022/07/ 23:03

OPPO A53
2022/07 5 23:03

Date
Page

S

Other features
→ ↓sed permeability of cell membrane
→ Dry skin with brittle nails.
→ Hair loss

** CALCIUM METABOLISM

→ already done in Bioc

DISEASES OF BONE

① OSTEOPHOROSIS → means porous bones
→ characterised by loss of bone matrix & minerals.

Causes → • occurs due to excessive bone resorption & ↓se bone formn.

• Common in women after 60 yr.

Risk factors →
- Sedentary life
- Genetic factor
- Early menopause / ovariectomy
- Excessive smoking
- Excessive alcohol / caffine intake
- High intake of protein

Manifestations → loss of bone matrix & minerals

↓

loss of bone strength

↓

Deterioration of bone tissue

↓

Bones become fragile with risk of fracture
↓
affected bones are vertebrae & Hip

② RICKETS

→ Bone disease in children
→ characterised by inadequate mineralisation of bone.
→ Occurs due to Vit. D defeciency
↓

- develop due to insufficiency in diet or due to inadequate exposure to light.
- affects the reabsorption of Ca & P from renal tubule, results in Ca defeciency

Causes :- · Vit D defeciency
· Renal disease

Features :- 1. Collapse of chest wall → deformity of chest with projecting sternum is c/d Pigeon chest
2. Kyphosis → Extreme forward curvature of upper back bone, c/d Humpback
3. Bowing of Hands & Legs
4. Enlargement of liver & spleen
5. Tetany

③ OSTEOMALACIA

→ Rickets in adult c/d osteomalcia

OPPO A53

Causes :- 1. Vit D defeciency
2. Renal diseases

Features :- 1. Vague pain
2. Tenderness in bones & muscles
3. Occasional Hypoglycamic Tetany

OPPO A53
2022/07/15 23:03

OPPO A53
2022/07/15 23:03

⑮ PANCREAS

→ INSULIN

- ★ Source → β-cells in islets of langerhans of pancreas

- ★ Plasma level → 10 u

Imp. ★ Synthesis → · Occurs in rough endoplasmic recticulum of β-cells of islets of langerhans.

बाकी का Bioc मे हैं।

↓

Synthesised as preproinsulin which converts into Proinsulin

↓

Proinsulin converted into Insulin + C-peptide

↓

through a series of peptic cleavages

C-peptide → · Connecting peptide that connects α & β - chains

· At time of secretion, C-peptide is attached.

$$\begin{tikzcd}
\text{Preproinsulin} \arrow[r] & \text{Pro-insulin} \arrow[d, "\text{Peptic Cleavage}"] \\
 & \text{Insulin}
\end{tikzcd}$$

★ Metabolism → · Degraded in liver & kidney by cellular enzymes c/d Insulin Protease / Insulin degrading Enzyme.

OPPO A53
2022/07/15 23:03

★ **Action**

v.Imp.

① On Carbohydrate Metabolism

→ Only antidiabetic Hr. in body

↓

reduces blood glucose level by following actions

i) ↑ses Transport & Uptake of glucose by cells

→ facilitates transport of glucose from blood into cells by ↑sing permeability of cell mem. to glucose

↓

Particularly Liver, Muscle & Adipose Tissue

Not required for glucose uptake in Brain, Renal Tubules, RBCs

→ ↑ses no. of glucose transporters, GLUT-4 in cell membrane

★ GLUT-4 → · insulin sensitive & located in cytoplasmic vesicle

- Ⓟnt in large no. in muscle fibre & adipose tissue
- when insulin-receptor complex is formed in mem.

↓

vesicle containing GLUT-4 released into mem.

↓

GLUT-4 start transporting the glucose molecule from ECF into the cell (at a faster rate).

ii) Promotes peripheral utilisation of glucose

→ In presence of insulin, glucose entering the cell utilised immediately.

Date ______
Page ______

iii) **Promotes storage of Glucose → Glycogenesis**

→ Promotes rapid conversion of glucose into glycogen
↓
stored in muscle & liver.

→ In liver, when glycogen content ↑ses beyond its storage capacity
↓
insulin causes conversion of glucose into fatty acid.

iv) **Inhibits Glycogenolysis**

→ prevents breakdown of glycogen into glucose in muscle & liver.

v) **Inhibits Gluconeogenesis**

→ prevents formn of glucose by inhibiting release of A.A. from muscle.

∴ Insulin ↓ses the blood glucose level by these five types of actions.

② On Protein Metabolism

→ facilitates the synthesis & storage of protein

→ Inhibits the cellular utilisation by following actions :-

i) facilitating transport of A.A. into cell from blood.
ii) Accelerating the protein synthesis
iii) Preventing protein catabolism
iv) Preventing conversion of protein into glucose

∴ Insulin ↑ses the conservation & storage of proteins

OPPO A53
2022/07/15 23:03

Date
Page

Imp.

(c) On fat Metabolism

→ Stimulates synthesis & storage of fat

→ Actions are :-

i) Synthesis of fatty acid & Triglycerides

→ Promotes transport of excess glucose into liver cells
↓
utilised for synthesis of fatty acid & triglycerides

→ Promotes synthesis by activating enzymes which converts :-
- Glucose into fatty acid
- Fatty acid into triglycerides

ii) Transport of fatty acid into adipose tissue → facilitate

iii) Storage of fat → Promotes storage in adipose tissue by inhibiting the enzyme which degrades triglycerides.

DISORDER RELATED TO INSULIN

200* ★ **DIABETES MELLITUS**

→ Metabolic disorder characterised by High Blood Glucose level.

→ Diabetes means Polyuria & Mellitus means Honey

→ There are several forms of diabetes mellitus, which occurs due to diff^n causes :-

① Type-I Diabetes Mellitus / Insulin-dependent Diabetes Mellitus (IDDM)

→ also K/n as juvenile onset diabetes.

→ Mainly occurs in childhood (b/w 12-15 yr. age).

→ Accounts for about 10-20% of K/n Diabetics.

OPPO A53
2022/07/15 23:03

OPPO A53
2022/07/15 23:03

→ Characterised by almost total defeciency of insulin due to destruction of β-cells of pancreas.

→ Destruction may be caused by Drug, Virus or Autoimmunity.

→ Due to certain genetic variation, β-cells are recognised as non-self & they are destroyed by immune mediated injury.

→ Symptoms appears when 80-90% of β-cells have been destroyed.

→ Pancreas fails to secrete insulin in respone to glucose ingestion

→ Patient require Insulin Therapy

→ Not associated with obesity but may associated with acidosis and ketosis.

Causes :– 1. Degeneration of β-cells in islets of langerhans
2. Destruction of β-cells by viral infection
3. Congenital disorder of β-cells.
4. Destruction of β-cells during autoimmune disease.

② Type-II Diabetes Mellitus / Non-Insulin-Dependent Diabetes Mellitus (NIDDM)

→ Also K/n as Adult Onset diabetes

→ Occurs in adult (usually above 35 yr.) & less severe then IDDM.

→ Account for about 80-90% of diabetic population.

→ Causative factors are genetic & Environmental

→ More commonly occurs in obese individual
↓
(overeating coupled with underactivity leads to NIDDM)

→ obesity act as a diabetogenic factor & leads to ↓se in insulin receptors on target cells.

→ Patient may have nrml or even ↑ed insulin level.

→ wt. reduction by diet control ⟶ often sufficient to correct NIDDM insulin resistance → impairing insulin receptor functions.

OPPO A53
2022/07/15 23:04

→ ↑sed level of • Tumor Necrosis factor - α (TNF - α)
• Resistin → (causes insulin resistance in obese people)

↓sed secretion of • Adiponectin by adipocytes

Causes :- 1. Genetic Disorders
2. Lifestyle changes such as bad eating, physical inactivity
3. Stress

** Signs and Symptoms of Diabetes Mellitus

→ Various manifestations develop b/c of 3 major setbacks of insulin defeciency :-

1. ↑sed Blood glucose level (300 to 900 mg/dl) due to reduced utilisation by tissue
2. Mobilisation of fat from adipose tissue for energy leads to elevated fatty acid content in blood.
3. Depletion of protein from tissue

igns & Symptoms :- 1. Glucosuria → Loss of glucose in urine when level rises above 180 mg/dl in blood.

2. Osmotic Diuresis → • diuresis caused by osmotic effect
• Excess glucose in renal tubule develops osmotic effect
↓
↓ses the reabsorption of water from tubules, resulting in diuresis & Leads to polyuria & polydipsia.

3. Polyuria → Excess urine formn with ↑se in ν of voiding urine.

OPPO A53

4. Polydipsia → • ↑se in water intake
   - Excessive loss of water ↓ses the water content & ↑ses the salt content in body.
   - This stimulates thrist center in hypothalamus, it ↑ses intake of water.

5. Polyphagia → • Means intake of excess food

6. Asthenia → • Loss of strength → body becomes very weak
   - Occurs due to protein depletion → caused by lack of insulin.

7. Acidosis → During insulin deficiency

   ↓

   Glucose cannot be utilised by tissue for energy

   ↓

   So, large amount of fat is broken down for energy

   ↓

   Causes formn of excess Ketoacids, leads to acidosis

other reason :- • Ketoacids are excreted in combination with Na^+ through urine (Ketonuria)

• Na^+ is exchange with H^+

↓

diffuses from renal tuble into ECF adding to acidosis

★ Acetone Breathing → • In severe acidosis, acetone is expired in expiratory air, giving the fruity breath odour.

• life - Threatening condn of severe diabetes

OPPO A53
2022/07 5 23:04

9. Circulatory Shock → • Osmotic diuresis leads to dehydration
↓
causes circulatory shock, occurs only in severe diabetes

** Complications of Diabetes Mellitus

1. Cardiovascular complications like :- Hypertension
Myocardial Infarction
2. Degenerative changes in Retina c/d Diabetic Retinopathy
3. Degenerative changes in Kidney c/d Diabetic Nephropathy
4. Degeneration of autonomic & peripheral nerves c/d Diabetic Neuropathy.

** Diagnastic Test for Diabetes Mellitus

1. Fasting Blood Glucose
2. Postprandal Blood Glucose
3. Glucose Tolerance Test (GTT)
4. Glycosylated (glycated) Hb.

** Treatment for Diabetes Mellitus

Type-1 → • Treated by Exogenous Insulin
↓

- Since Insulin is polypeptide → gets degrade in GIT if taken orally.
- So, administered by subcutaneous injection

OPPO A53
2022/07/15 23:04

Type - II → • Treated by oral Hypoglycemic drug

• Patients with long lasting severe diabetes may require

↓

combination of oral hypoglycemic drug with insulin

↓

to control Hyperglycemia

** REGULATION OF BLOOD GLUCOSE LEVEL (BGL)

→ In early morning, after overnight fasting

↓

Blood glucose level is low b/w **70 to 110 mg/dL**

→ B/w 1st & 2nd hr. after meal [postprandal]

↓

Blood glucose rises from **100 to 140 mg/dL**

→ Glucose level in blood is bought to nrml at end of 2nd hr. after the meal.

→ Blood glucose regulating mechanism is operated through liver & muscle by influence of pancreatic Hr. → Insulin & Glucagon

→ Among all the hormones, insulin is only hr. that reduces blood glucose level so c/d **Antidiabetogenic Hr.** & which ↑es blood glucose level are c/d **Diabetogenic Hr.** | Anti-Insulin Hr.

1. Role of liver in maintenance of BGL

→ Serves as an imp. glucose Buffer system

Date ____
Page ____

→ when blood glucose level ↑ses after a meal
↓
Excess glucose is converted into glycogen & stored in liver

Afterwards, when level ↓ses
↓
glycogen in liver is converted into glucose & released in blood.

∴ Storage of glycogen & release of glucose mainly regulated by insulin & glucagon

2. Role of Insulin

→ Insulin ↓ses BGL & is only antidiabetic Hr.
बाकी, Action of Insulin on carbo. metabolism लिखना है।

3. Role of Glucagon

→ ↑ses BGL by :-
1) ↑sing glycogenolysis in liver [does not induce glycogenolysis in muscles]
2) ↑sing gluconeogenesis

4. Role of other Hormones

other which ↑ses BGL are :-
1. Growth Hr.
2. Thyroxine
3. Cortisol
4. Adrenaline

OPPO A53
2022/07 5:23:04

ADRENAL CORTEX

→ Adrenocorticotrophic Hr. are steroid in nature, hence named Corticosteroid.

→ classify in 3 grps :-

a) Mineralocorticoids

→ Acts on minerals :- Na^+ & K^+

→ Mineralocorticoids are :- Aldosterone

Source :- Zona glomerulosa

Functions

i) Life Saving Hr.

→ Very essential for life & it maintains the osmolarity & vol. of ECF.

→ c/d life saving b/c absence causes death within 3 days to 2 ~~days~~ weeks :

Cholesterol
↓ ⟶ cholesterol desmolase
Pregnenolone
↓ ⟶ 3 β - Hydroxysteroid dehydrogenase
Progesterone
↓ ⟶ 21 β - Hydroxylase
11 - deoxycorticosterone
↓ ⟶ 11 β - Hydroxylase
Corticosterone
↓ ⟶ 18 β - Hydroxylase & 18 - dehydroxydehydrogenase
Aldosterone

Synthesis

OPPO A53
2022/07/15 23:04

* Aldosterone acts on Principal cells of C.D.

→ Has 3 functions :- 1. Reabsorption of Na^+ from renal tubule ↑ses
2. Excretion of K^+ through renal tubule
3. Secretion of H^+ into renal tubule

1. On Na^+ ions

→ Acts on DCT & CD & ↑ses Reabsorption of Na^+.

During Hypersecretion :- loss of Na^+ through urine ↓ses & is only few milligms per day.

During Hyposecretion :- Loss of Na^+ through urine ↑ses (Hypernatriuria)

2. On ECF volume

→ when Na^+ are reabsorbed ⟶ • simultaneously water is also reabsorbed.

Even though aldosterone ↑ses Na absorption from renal tubule
↓
Conc. of Na in body does not ↑ses b/c water is also reabsorbed simultaneously

3. On Blood Pressure

→ Increase in ECF vol. & Blood vol, ↑ses BP.

Excess Aldosterone ⟶ ↑sed Na^+ reabsorption by tubules
↓
simultaneously osmotic absorption of equal amount of H_2O
↓
ECF vol ↑ses without much change in Na^+ conc.

OPPO A53
2022/07/15 23:04

Date
Page

Deficiency of Aldosterone

↑se in K^+ conc. in ECF
↓
Cardiac Toxicity
↓
Arrhythmia
↓
Cardiac death

↓se in Na^+ & Cl^- conc. in ECF
↓
↓se in ECF volume
↓
↓se in blood volume
↓
Cardiac dysfunction
↓
Circulatory Shock

★ ALDOSTERONE ESCAPE

→ Escape of kidney from salt-retaining effects of excess administration or secretion of aldosterone.

→ Aldosterone mediated ↑se in ECF vol. lasting more then 1-2 days leads to ↑se in Arterial B.P.

↓

↑ses kidney excretion of Both Na^+ & H_2O c/d Pr. Natriuresis & Pr. Diuresis resp.

↓

this elevated BP returns the renal output of Na^+ & H_2O to nrml despite the excess aldosterone

↓

& is c/d Aldosterone Escape

∴ Rate of gain of Na^+ & water by body is 0 & a balance is maintained b/w Na-water intake & output by kidney despite continued excess Aldosterone.

OPPO A53
2022/07/15 23:04

↑sed Aldosterone level

↓

Reabsorption of excess Na & water from renal tubule

↓

↑se in ECF volume

↓

↑se in atrial B.P.

↓ ↓

Secretion of ANP from atrial muscles | Pr. natriuresis & diuresis

↓

Excretion of Na^+ & H_2O through urine

↓

↓sed ECF volume

4. On K^+ ion

→ It ↑ses the K^+ excretion through renal tubule.

→ When aldosterone is deficient,

K^+ conc. in ECF ↑ses leading to Hyperkalemia

↓

Results in serious cardiac ~~Hyperkalemia~~ toxicity

↓

weak contraction of heart & development of arrhythmia

↓

In severe condⁿ, causes cardiac death

→ When aldosterone secretion ↑ses, leads to Hypokalemia & muscular weakness.

OPPO A53
2022/07/15 23:04

Date
Page

5. On H^+ ion

- While ↑ing Na - reabsorption, it causes tubular secretion of Hydrogen ion.

↓

reduces H^+ - conc. in ECF

→ In nrml condⁿ, aldosterone is essential to maintain acid-base balance in body.

→ In Hypersecretion, causes alkalosis & in Hyposecretion causes acidosis.

6. On sweat & salivary glands

→ ↑ses reabsorption of Na & Excretion of K^+ by excretory duct of sweat & salivary gland.

7. On Intestine

↑ses Na^+ absorption by intestine, especially from colon & prevents loss of Na^+ through stool.

** REGULATION OF SECRETION

→ Regulation by zona glomerulosa is almost entirely independent of regulation of cortisol & androgens by zona fasciculata & zona reticularis.

→ Secretion is regulated by 4 imp. factors which are given in order of their potency :-

OPPO A53
2022/07/15 23:04

1. ↑se in K+ ion conc. in ECF
2. ↓se in Na+ ion conc. in ECF
3. ↓se in ECF volume
4. **Adrenocorticotrophic Hr. (ACTH)**

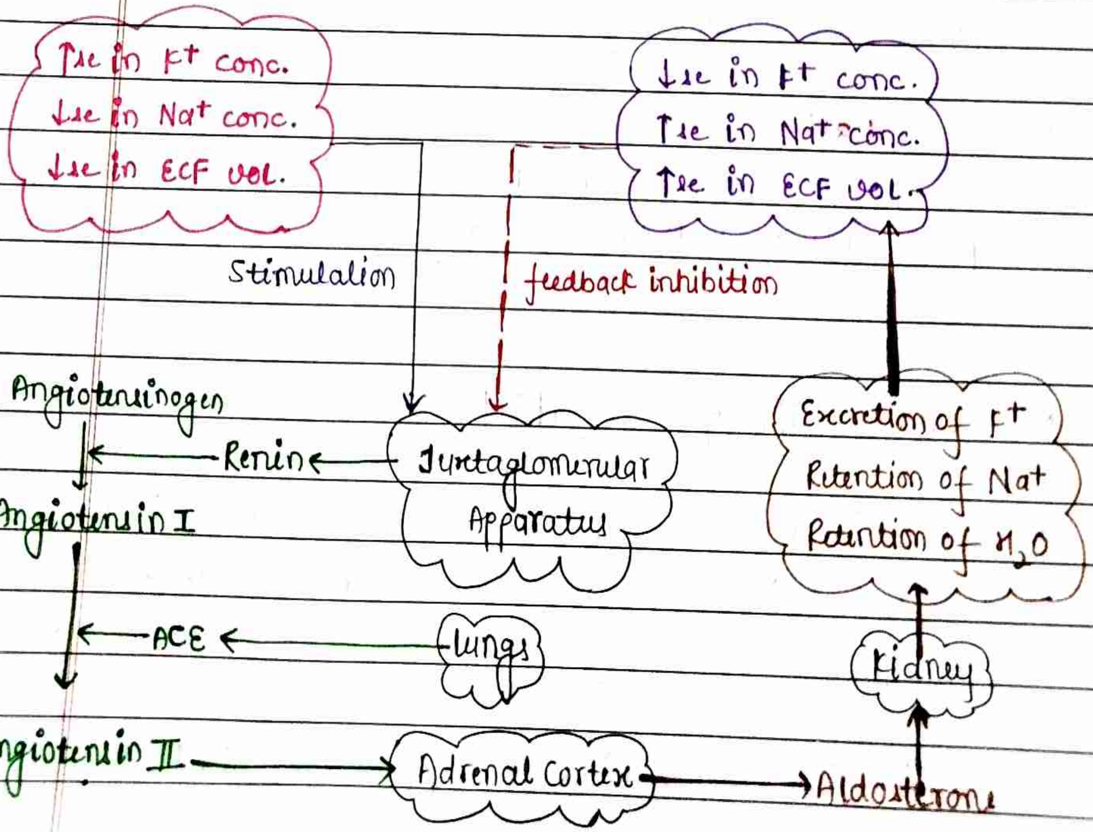
→ ↑sed in K+ ion conc. ⟶ ↑ses aldosterone secretion

→ ↑sed Angiotensin II conc. ⟶ —— " ——

→ ↑sed Na+ ion conc. ⟶ very slightly ↓ses aldosterone secretion

→ ACTH from Ant. Pituitary ⟶ Has little effect in controlling the rate of secretion

★★ K+ ion conc. & RAAS are very / most potent in regulating aldosterone secretion


↑se in K+ conc.
↓se in Na+ conc.
↓se in ECF vol.
Stimulation
↓se in K+ conc.
↑se in Na+ conc.
↑se in ECF vol.
feedback inhibition
Angiotensinogen
Renin
Juxtaglomerular Apparatus
Angiotensin I
ACE
Lungs
Angiotensin II
Adrenal Cortex
Aldosterone
Kidney
Excretion of K+
Retention of Na+
Retention of H2O

Date ______
Page ______

b) Glucocorticoids

→ Acts mainly on glucose metabolism
→ Include :- 1. Cortisol (95% activity)
2. Corticosterone (4% activity)
3. Cortisone (1% activity)

* Source :- • Mainly by Zona fasciculata of adrenal cortex

* Synthesis :-

Cholesterol
↓ ← cholesterol desmolase
Pregnenolone
↓ ← 17 α - hydroxylase
17 - Hydroxypregnenolone
↓ ← 3 β - Hydroxysteroid dehydro-genase
Progesterone → 17 - Hydroxyprogesterone
↓ ← 21 β - Hydroxylase
11 - deoxycortisol
↓ ← 11 β - Hydroxylase
Cortisol

Imp. * **Functions**

Life Protecting Hormone
Aldosterone is life saving Hr.
Cortisol → life protecting Hr. b/c Helps to withstand stress & trauma in life

Exposure to even mild harmful stress after Adrenalectomy leads to collapse & death.

OPPO A53
2022/07/·5 23:05

Date
Page

On Carbohydrate Metabolism

→ ↑ses blood glucose level by 2 ways :-

i) By promoting gluconeogenesis in liver

→ enhances breakdown of protein in extrahepatic cells particularly muscles

↓

followed by release of A.A. into circulation

↓

from blood A.A. enters liver & converted into glucose

ii) By inhibiting the uptake & utilisation of glucose by peripheral cells → • This is anti-insulin action of cortisol

↓

It ↓ses translocation of GLUT-4 to the cell membrane, especially skeletal muscle cells, leading to Insulin Resistance

2. On Protein Metabolism

→ ↑ses catabolism of proteins & leads to :-

- i) ↓se in cellular protein
- ii) ↑se in plasma level of A.A.
- iii) ↑se in protein content in liver

→ ↑se catabolism by following method :-

i) By releasing A.A. from body cells, into blood (except liver)

ii) By ↑sing uptake of A.A. by liver cells from blood

↓

A.A. used for synthesis of Protein & Carbohydrate

OPPO A53
2022/07/15 23:05

→ In oversecretion, there is excess catabolism of proteins results into muscular wasting & (-)ve N-balance

3. On fat Metabolism

→ causes mobilization and redistribution of fat

→ Actions on fat are :-

i) Mobilization of fatty acid from adipose tissue
ii) ↑ing conc. of fatty acid in blood
iii) ↑ing utilisation of fat for energy

→ Glucocorticoids, ↓se the utilisation of glucose

↓

at same time make fatty acid available for use

↓

by which energy is generated &

↓

leads to form^n of large amount of ketone bodies

↓

c/d **ketogenic effect**

→ Hyposecretion causes → abnrml type of obesity

↓

by ↑ing deposition of fat in certain areas such as abdomen, chest, face & buttocks

4. On Resistance to Stress

→ Exposure to any type of stress (physical / mental)

↓

↑se secretion of Adrenocorticotrophic Hr. (ACTH)

↓

OPPO A53
2022/07/15 23:05

↑se glucocorticoids secretion

↓

essential for survival during stress, as it offers high resistance to the body against stress.

→ Enhance resistance by following ways :-

1. Release & Transport of A.A. from tissue to liver cells

↓

for synthesis of proteins & other substances

↓

essential to withstand the stress.

2. Release of fatty acid from cell

↓

for production of energy during stress

3. Enhancement of vascular response to catecholamines & fatty acid-mobilization action of catecholamines

↓

necessary to withstand stress

5. Antiallergic Action

→ Corticosteroids prevents various rx^n in allergic $cond^n$, as in inflammation.

6. Immunosuppressive Effect

→ Suppress the immune system by ↓sing the no. of T-cells & also prevents the release of IL-2 by T-cells.

→ Hypersecretion → ↓ses the immune rx^n against all foreign bodies, leads to severe infection & death.

OPPO A53
2022/07/15 23:05

→ During Organ Transplantation → are used to supress the immunological rx^n b/c of their immunosuppressive action.

7. Anti-Inflammatory Action

→ Prevents inflammatory changes by :-

1. Inhibiting release of chemical sub. from damaged tissue, thus preventing vasodilation & erythemia (rushing of blood)
2. Causing vasoconstriction through catecholamines
3. ↓sing the permeability of capillaries & preventing loss of fluid from plasma into affected tissue.
4. Inhibiting migration of leukocytes into affected area.
5. Suppressing T-cells, so there is reduction in rx^n of tissue which enhance the inflammatory process.

Imp. ★ MODE OF ACTION

already done

★★ REGULATION OF SECRETION

→ Ant. Pituitary regulates secretion by ACTH
→ ACTH regulates by hypothalamus through → CRF (corticotropin releasing factor)

① Role of Ant. Pituitary
Controls the activity of adrenal cortex by secreting ACTH.
↓
ACTH mainly concerned with regulation of cortisol secretion & has minor role in mineralocorticoid secretion.

OPPO A53
2022/07/15 23:05

Date
Page

* ACTH → • Secreted by Basophilic chromophilic cells of ant. pituitary.

- Synthesised from a protein c/d Prepro-opiomelano-cortin (POMC).

Actions → • Necessary for structural integrity & secretory activity.

- Actions on Adrenal Cortex are :-

1. Maintenance of structural integrity & vascularization of zona fasciculata & zona reticularis.
2. Helps in synthesis of glucocorticoids.
3. Release of glucocorticoids.
4. Prolongation of glucocorticoid action on various cells.

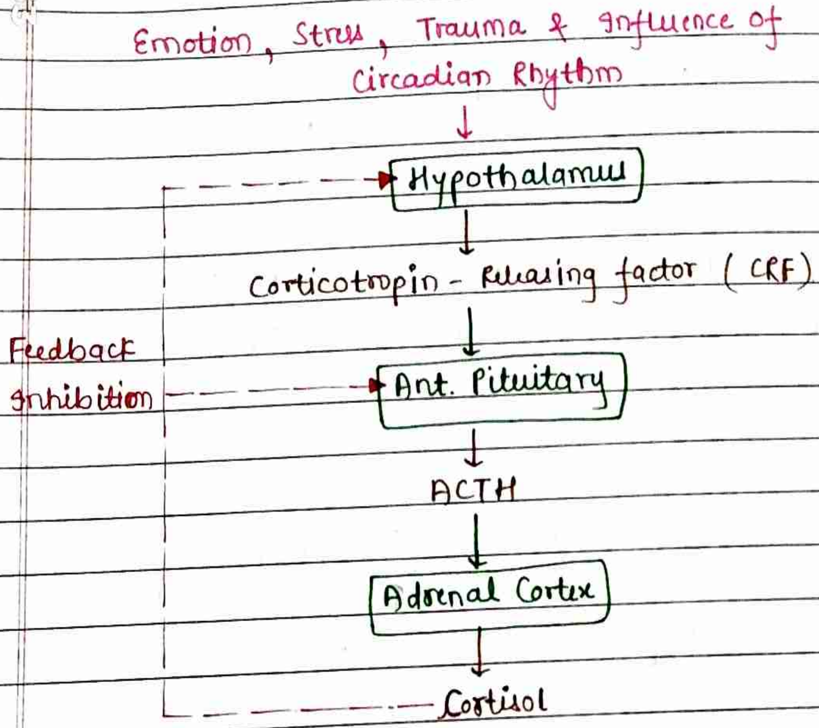
② Role of Hypothalamus

→ Plays an imp. role in cortisol secretion by controlling ACTH secretion through CRF.
↓

- reaches ant. pituitary through Hypothalamo-Hypophyseal portal vessels.
- stimulates corticotrophs of ant. pituitary & cause synthesis & release of ACTH.
- CRF secretion is induced by several factors such as emotion, stress, trauma & circadian rhythm.

③ Feedback Control

Cortisol regulates its own secretion through negative feedback control by inhibiting the release of CRF from hypothalamus & ACTH from ant. pituitary.


Emotion, Stress, Trauma & Influence of Circadian Rhythm
Hypothalamus
Corticotropin - Releasing factor (CRF)
Ant. Pituitary
ACTH
Adrenal Cortex
Cortisol
Feedback Inhibition

* Regulation of Cortisol Secretion

OPPO A53
2022/07 5 23:05

Date
Page

OPPO A53

100*

CUSHING'S SYNDROME

→ Disorder characterised by obesity

Causes → • due to Hypersecretion of Glucocorticoids
↓
particularly cortisol

- If due to pituitary origin ⟶ Cushing's disease
- If due to Adrenal origin ⟶ Cushing's syndrome

1. Pituitary Origin

→ ↑sed secretion of ACTH causes hyperplasia of adrenal cortex
↓ [↑se in no. of cells]
leads to hypersecretion of gluco-corticoids

*** ACTH secretion is ↑sed by :-**

i) Tumor in pituitary cells.
ii) Malignant tumor of non-endocrine origin
iii) Hypothalamic disorder causing hypersecretion of CRH.

2. Adrenal Origin

*** Cortisol Secretion is ↑sed by :-**

i) Tumor in zona fasciculata
ii) Cancer in adrenal cortex
iii) Prolonged treatment with high doses of ACTH, which stimulates cortex to secrete excess gluco-corticoids.

OPPO A53
2022/07/ 5 23:05

* Signs & Symptoms

i) Characteristic feature → disproportionate distribution of body fat, resulting in abnorml features :-
Moon face → edematous facial expression
Torso → fat accumulation in chest & abdomen
Buffalo bump → fat deposit on back of neck & shoulder.
Pot belly → fat accumulation in upper abdomen.

ii) Purple Striae → Reddish purple strips on abdomen
iii) Thining of extremities
iv) Pigmentation of skin especially in ACTH - dependent type due to hypersecretion of ACTH (has got melanocyte stimulating effect).
v) Weakning of bones, bone resorption & osteoporosis due to protein depletion.
vi) Weakning of muscles b/c of protein depletion.
vii) Hypertension by the mineralocorticoids effects of glucocorticoids.
* Hirsutism → heavy growth of body & facial hairs.
viii) Immunosppression → cause susptibility for infection
ix) Poor wound healing
x) Facial plethora → facial redness.

* Tests for Cushing Syndrome

i) Observation of external features.
ii) Determination of blood sugar & cortisol level
iii) Analysis of urine.

★ Treatment

i) ↓ ACTH production
Hypophysectomy → removal of pituitary gland
Radiation

ii) ↓ Adrenocortical cortisol Secretion
Bilateral Adrenalectomy
Medical Adrenalectomy

★ ADDISON'S DISEASE

→ also k/n as Hypoadrenalism

→ Causes

Results from an inability of the adrenal cortices to produce sufficient adrenocortical Hr. & this in turn is most frequently caused by 1° atrophy (↓se in size) of adrenal cortices

→ Signs & Symptoms

i) Weakness of muscles
ii) Pigmentation of skin & mucous membrane due to excess ACTH secretion.
iii) Dehydration with loss of Na^+
iv) Hypotension
v) Wt. loss
vi) Nausea, Vomiting & diarrhea.
vii) ↓sed cardiac output & ↓sed workload of heart
viii) Abdominal pain

OPPO A53

OPPO A53
2022/07

Date
Page

* Test for Addison's Disease

i) Measurement of blood level of ~~glucose~~ cortisol & aldosterone.

ii) Measurement of amount of steroids excreted in urine

* Treatment

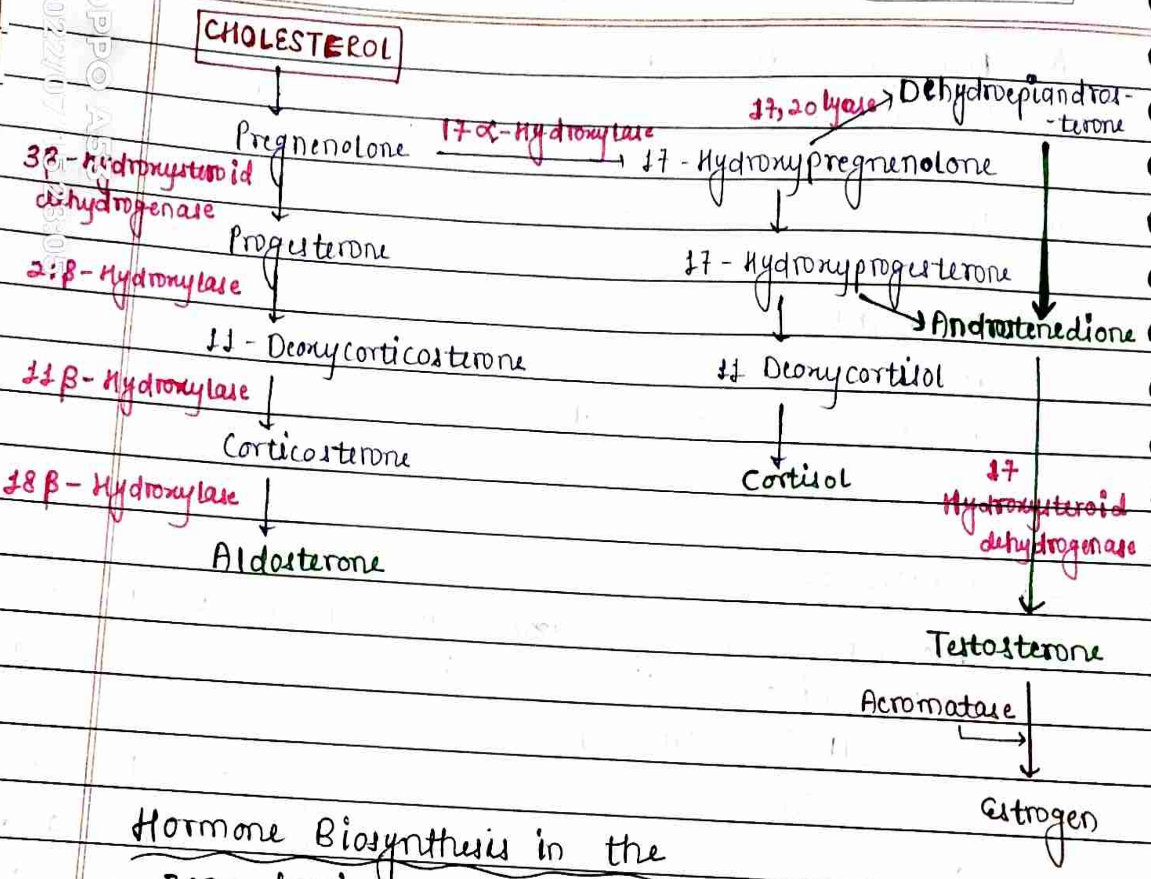
Person can live for years if small quantity of mineralocorticoids & gluco-corticoids are administered daily.

→ Addisonian Crises

→ The critical need for extra glucocorticoids & the associated severe debility in times of stress is c/d Addisonian Crisis
[Physical weakness]

→ Adrenal Crises → common symptom of adrenal disease/ addisons disease, characterised by sudden collapse and associated with an Ise in need for large quantities of glucocorticoids

→ Causes → i) Exposure to even mild stress
ii) Hypoglycemia due to fasting
iii) Trauma
iv) Surgical operation
v) Sudden withdrawal of glucocorticoid treatment


CHOLESTEROL
Pregnenolone
3β-Hydroxysteroid dehydrogenase
Progesterone
21β-Hydroxylase
11-Deoxycorticosterone
11β-Hydroxylase
Corticosterone
18β-Hydroxylase
Aldosterone
17α-Hydroxylase
17-Hydroxypregnenolone
17,20 lyase
Dehydroepiandrosterone
17-Hydroxyprogesterone
Androstenedione
11 Deoxycortisol
Cortisol
17 Hydroxysteroid dehydrogenase
Testosterone
Acromatase
Estrogen

Hormone Biosynthesis in the zona fasciculata & Reticularis

Date ______
Page ______

CARDIOVASCULAR SYSTEM ***

① PROPERTIES

1. Autorhythmicity

→ The ability of heart to initiate its beat continuously & regularly without external stimulation.

→ Heart is myogenic → independent of nerve supply

→ due to specialized excitatory & conductive system of heart

↓

wave of depolarization generates

↓

cardiac impulses

★ **Autorhythmic fibres** → • forms 1% of cardiac muscle fibres

• Has 2 imp functions :-

Act as Pacemaker → set the rhythm of electrical excitation

Forms the conductive system → network of specialized cardiac muscle fibres.

★ Location of Autorhythmic cells

1. Sinoatrial Node (SA-Node) → At right atrial wall near opening of SVC.

2. Atrioventricular Node (AV-Node) → At base of Rt. Atrium near septum

3. Bundle of His → Cells originate at AV Node & enter

OPPO A53
2022/07/1 5:28:05

OPPO A53
2022/07/15 23:06

interventricular septum
↓
divide into Rt & Lt bundle branches
↓
- travel down septum, curve around tip of ventricular chamber.
- Travel back towards atria along outer wall.

9. Purkinje fibres → · Terminal fibres, extend from bundle of His
   - Spread throughout ventricular myocardium.

Imp ★ **Pacemaker & Pacemaker Potential**

→ Pacemaker → · St. of heart from where the impulses for heartbeat are produced.
   - In mammals, pacemaker is SA - Node.

→ Pacemaker Potential → · Unstable RMP in cells of SA node.
- Electrical Potential in SA node is different from that of other cardiac muscle fibres.
- RMP in SA node cell has negativity of -55 to -60 mV.

★ **Ionic Basis of Electrical Activity**

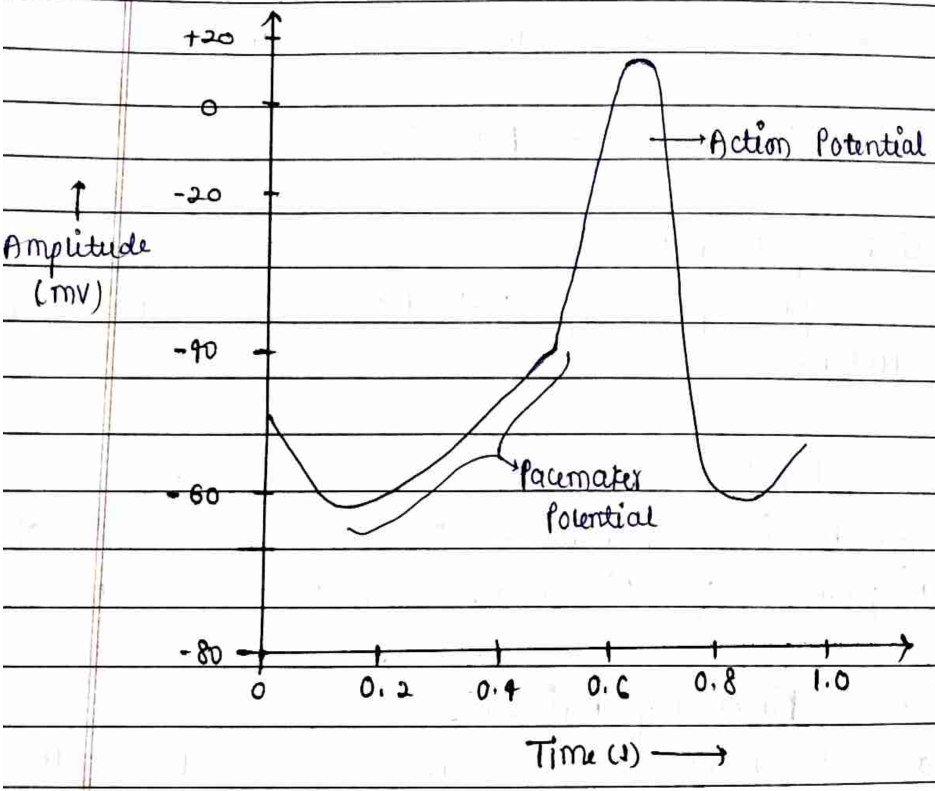
Sodium ion leaks into the pacemaker fibres
↓
causes slow depolarisation & forms initial part of pacemaker potential
↓
Ca^{++} channel starts opening

OPPO A53
2022/07 23:06

↓

At beginning, slow influx of Ca^{++} ions
↓
causing further depolarization & forms later part of pacemaker potential

∴ Initial part is due to → Slow Influx of Na^{+} ions.
later part is due to → Slow Influx of Ca^{++} ions.



Part of Heart	Rate of generation of Impulse
SA node	70 mph
AV node	50 mph
Purkinje fibres	30 mph

OPPO A53
2022/07/15 23:06

② Excitability

→ The ability of cardiac muscle to respond to a stimulus of adequated st. & duration by generating an AP.

AP initiated by SA node

↓

Travels along conductive pathway

↓

Excites atrial & ventricular muscle fibres

Imp. ★★

Ionic Basis of Action Potential

1. Initial depolarisation

→ B/c of rapid opening of Na^+ channels & rapid influx of Na^+ ion.

2. Initial Repolarisation

→ B/c of transient opening of K^+ channel & efflux of small quantity of K^+ ions, from the muscle fibres.

3. Plateau / Final Depolarisation

→ B/c of Ca^{++} inflow when voltage gated slow Ca^{++} channel open and some K^+ – channel closes.

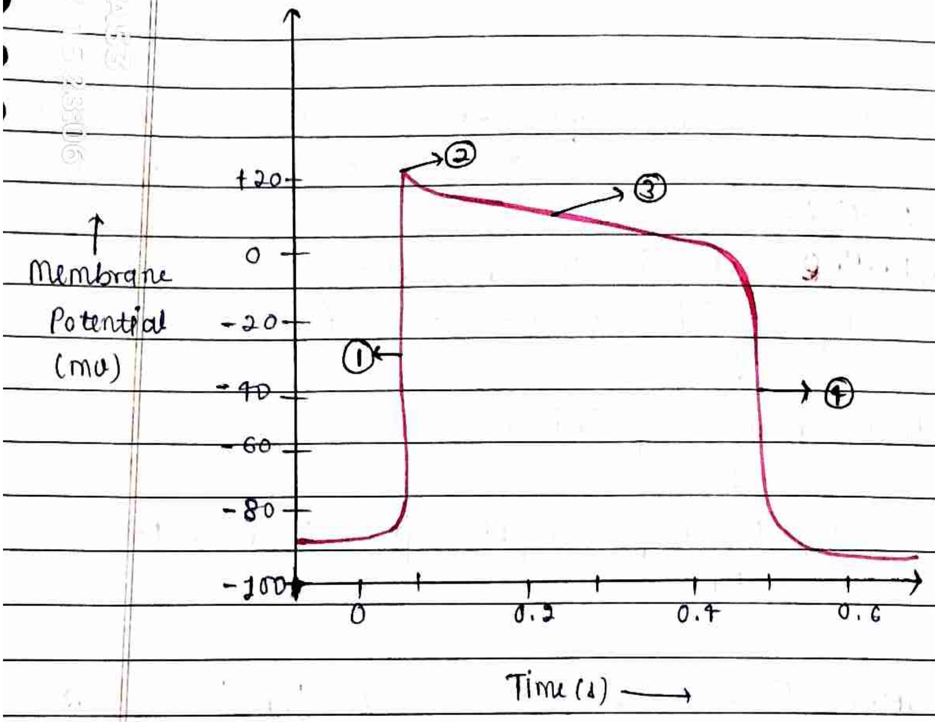
→ Ca^{++} entering the muscle fibre plays an important role in contractile process.

4. ~~Plateau~~ Final Repolarisation

→ B/c of efflux of potassium ion

→ No. of K^+ ions moving out exceeds the no. of Ca^{++} ions moving in, makes negativity inside.

→ Resulting in final Repolarisation.



★ **Spread of AP through Cardiac muscle**

AP Spread through Cardiac muscles very rapidly

↓

b/c of presence of Gap junction b/w cardiac muscle fibres

↓

Gap junctions are permeable & allow free movements of ions & so the AP spreads rapidly from 1 fibre to another

↓

AP is transmitted from atria to ventricles through the fibres of specialised conductive system.

OPPO A53
2022/07/15 23:06

Date
Page

3. **Contractility**

→ ability of cardiac muscle to contract in response to stimulation.

Excitation contraction coupling → same as of skeletal muscle
(वही वाला लिखना है)

4. **Conductivity**

★ **Conductive system in Human Heart**

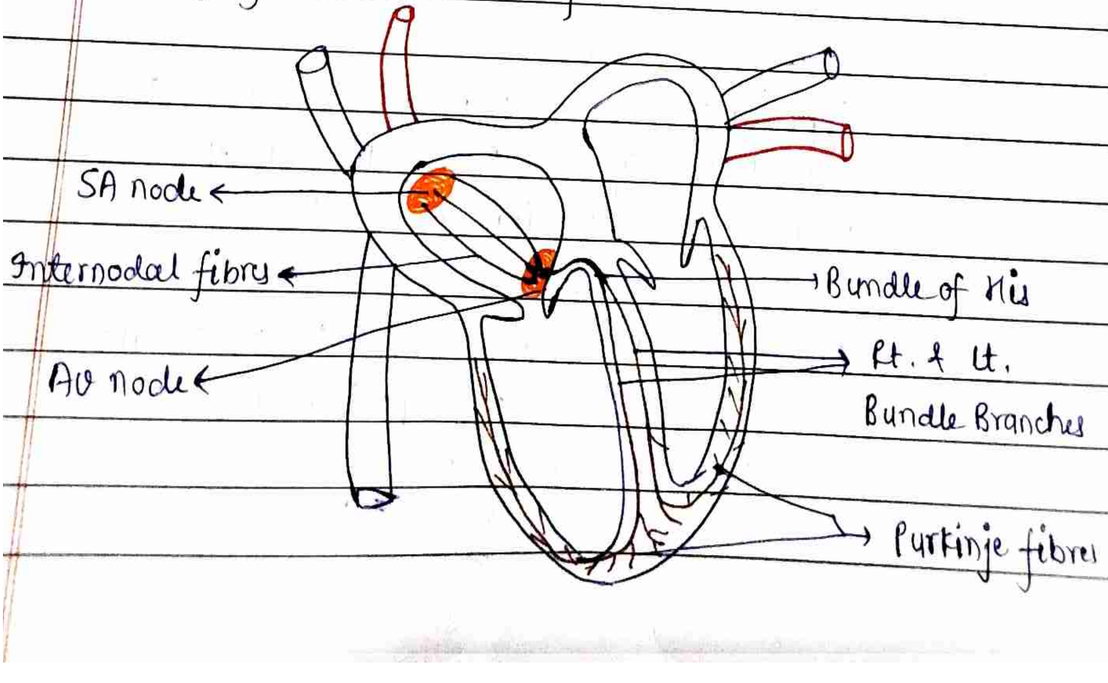
→ Formed by modified cardiac muscle fibres
↓
these fibres are specialized cells
↓
conducts the impulse rapidly from SA node to ventricles

Conductive tissue of Heart → Cd as Junctional Tissue

★ **Components**

- → AV node
- → Bundle of His
- → Rt. & Lt. bundle branches
- → Purkinje fibres

} सभी को describe भी कर देना



SA node
Internodal fibres
AV node
Bundle of His
Rt. & Lt. Bundle Branches
Purkinje fibres

OPPO A53
2022/07/15 23:06

Date ______
Page ______

OPPO A53
2022/07/15 23:06

Impulse from SA node is donducted throughout Rt. & Lt. atria

↓

Then, reaches to AV node through specialised internodal fibres

↓

Then, to Bundle of His

↓

from each br. of Bundle of His

↓

many purkinje fibres arises & spread impulse all over the ventricular myocardium.

3. Contractility

→ **Following** are the contractile properties :-

1. **All or None law**

when a stimulus is applied whatever may be the st.

↓

Whole cardiac muscle gives maxm response or it does not give any response at all

2. Staircase Phenomena

when the ventricle of heart is stimulated at interval of 2 seconds, without changing the st.

↓

force of contraction ↑es gradually for 1st few seconds, then it remains same.

↓

Gradual increase in **force** of contraction is c/d Staircase Phenomena

OPPO A53
2022/07/ 5 23:06

**Some ②

CARDIAC CYCLE

→ Defined as the succession of coordinated events taking place in heart during each beat.

→ Duration → when heart beat is 72 beats / min
↓
duration of each cardiac cycle is about 0.8 seconds.

In clinical practice :- Systole → Ventricular Systole
Diastole → ventricular diastole

★ Atrial Events

1. Atrial Systole (0.1 sec)

→ also c/d last rapid filling phase of presystole.
↓
considered as last phase of ventricular diastole

→ During this period only a small amount i.e., 10%. of Blood is forced from A → V

→ Non-essential for maintainance of circulation
↓
many persons with atrial fibrillation survive for yrs.

4th Heart Sound

contraction of atrial musculature causes 4th H.S.

OPPO A53
2022/07/15 23:06

Atrial Diastole (0.7 sec)

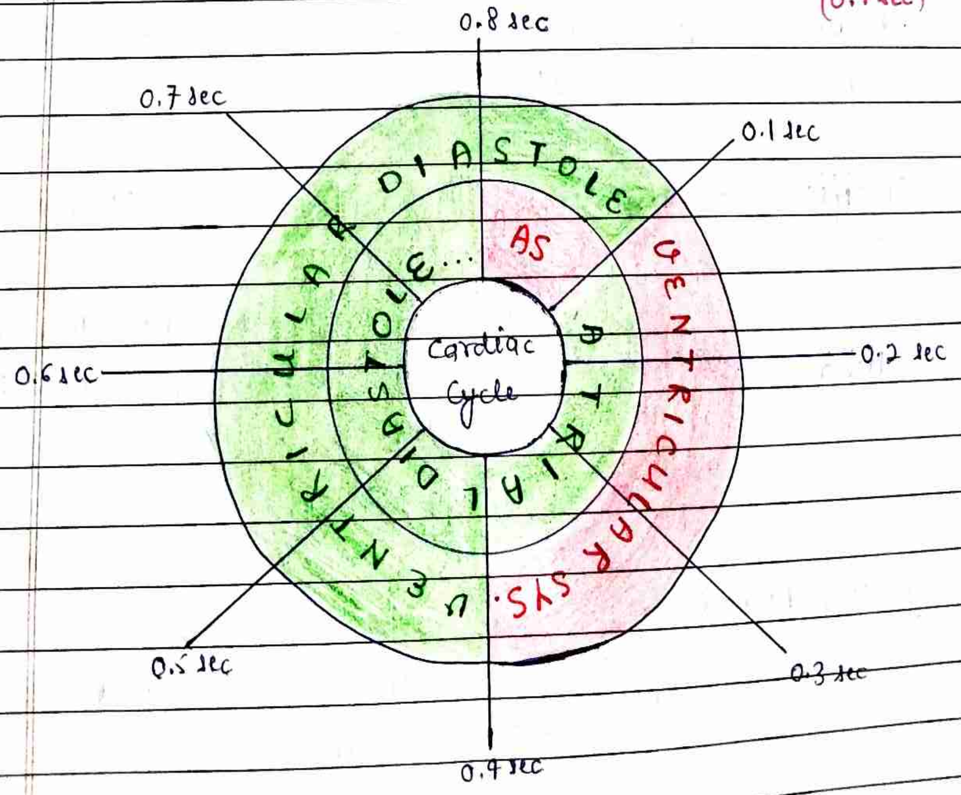
After systole, atrial diastole starts
↓
simultaneously ventricular systole also starts

→ This is the period during which atrial filling takes place.

→ Rt. atrium → receives deoxygenated blood from SVC & IVC.
Lt. atrium → receives oxygenated blood from pulmonary veins

	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8
A →	S	D	D	D	D	D	D	D
V →	D	S	S	S	D	D	D	D

↓
common diastole for (0.4 sec)


0.8 sec
0.1 sec
0.2 sec
0.3 sec
0.4 sec
0.5 sec
0.6 sec
0.7 sec
DIASTOLE
AS
VENTRICULAR SYS.
ATRIAL DIASTOLE...
VENTRICULAR
Cardiac Cycle

Date
Page

★ Ventricular Events

Ventricular Systole

1. Isometric Contraction / Isovolumetric Contraction

→ 1st phase of ventricular systole

→ Type of muscular contraction, characterised by ↑se in tension without any change in length of muscle fibres.

→ Immediately after atrial systole, AV valves are closed
Semilunar valves are already closed

↓

Now, ventricles contracts as a closed cavities in such a way that there is no change in volume of ventricular chambers.

1st Heart Sound

Closure of AV valve at beginning of Isometric Contraction causes 1st H.S.

Significance → responsible for opening of Semilunar Valves

↓

As ventricular pr. ↑ses & when this Pr. becomes more then the pr. in aorta & Pulmonary Ar.

↓

Semilunar valves opens

2. Ejection Period

Due to opening of semilunar valves & isotonic contraction of ventricles

↓

Blood is ejected out from both the ventricles

OPPO A53
2022/07 5 23:06

OPPO A53
2022/07 5 23:06

Date
Page

★ **Has 2 stages :-**

1. First stage or Rapid Ejection Period
   - → Starts immediately after the opening of semilunar valves
   - → Large amount of blood is rapidly ejected from both ventricles.

2. Second stage or Slow Ejection Period
   - → Blood is ejected slowly with much less force.

★ Ejection fraction

$$E_f = \frac{EDV - ESV}{EDV} = \frac{SV}{EDV} = \underline{60 \text{ to } 65\%}$$

Significance :- • measurement of lt. ventricular functions
- imp index for assessing ventricular contractility.
- ↓es in myocardial infarction & cardio-myopathy.

→ End-Diastolic Volume &	End-Systolic Volume
↓	↓
amount of blood remaining in each ventricle at the end of diastole.	amount of blood remaing in each ventricle at the end of systole
about → 130 to 150 ml	about → 60 to 80 ml

OPPO A53
2022/07/15 23:06

Ventricular Diastole

1. Protodiastole

→ Due to ejection of blood, pr. in ventricles ↓ses
→ when intraventricular pr. becomes less then pr. in aorta & pulmonary Ar., semilunar valves closes.

→ This phase, indicates only the end of systole & beginning of diastole

2nd Heart Sound
due to closure of semilunar valve

2. Isometric Relaxation Period

→ Type of muscular relaxation, characterized by ↓se in tension without any change in length of muscle fibre.

→ once again all the valves are closed, both the ventricles ~~stays~~ relax as closed cavities without any change in volume. So, c/d Isovolumetric Relaxation.

Significance :- Responsible for opening of AV valves
↓
As ventricular Pr. ↓ses & becomes less then the pr. in atria
↓
AV-valves opens.

3. Rapid filling phase

→ Sudden rush of blood from atria into ventricle

* About 70% of filling takes place during this phase

Date
Page

3. Slow filling Phase (also c/d Diastasis)
ventricular filling becomes slow
* About 20% of filling occurs in this phase

4. last Rapid filling Phase
→ Occurs b/c of Atrial Systole, atria contract & pushes a small amount of blood into ventricles, c/d **Atrial Kick**
* About 10% of filling occurs in this phase

Events of Cardiac Cycle

Isovolumetric Contraction
- All valves are closed
- No change in chamber size
- Ventricles undergo contraction & Pr. ↑ses.

Ejection
- Semilunar valves are open
- AV valves are closed
- Ventricles contracts & blood is ejected out.

Isovolumetric Relaxation
- All valves are closed
- No change in chamber size
- Ventricle undergo relaxation & Pr. ↓ses.

Filling (Rapid & Slow)
- AV valves are opened
- Blood enters ventricles from atria.
- ↑se in ventricular size

Atrial Systole
- Atria contract & a small amount of blood enters the ventricle
- Atrial size ↓ses

OPPO A53
2022/07/15 23:06

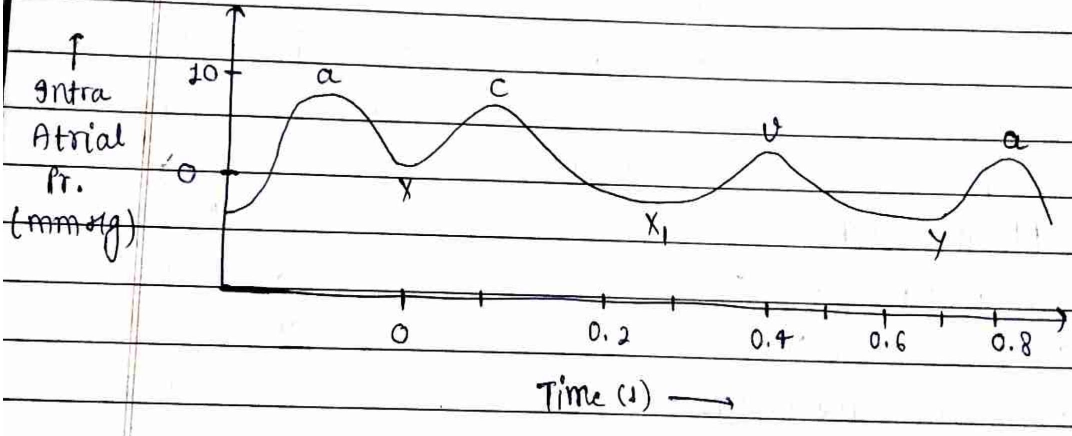
Date
Page

★ Intra-Atrial Pr. change during Cardiac Cycle

→ **Significance** :- • Intra-atrial Pr. is responsible for opening of AV values
• Main factor for development of venous pulse.

→ **Method of Study** :- Rt. Atria → cardiac catheterization (directly recorded)
Lt. Atria → Pulmonary Capillary Wedge Pr. (indirectly)

→ **Intra Atrial Pr. Curve**



(+) a wave → atrial systole
(−) x wave → atrial diastole → relaxation occurs, Pr. falls
(+) c wave → Isometric contraction (closure of AV value)
(−) x, wave → Ejection period
(+) v wave → atrial diastole → filling of blood occurs, Pr. ↑ses
(−) y wave → Isometric Relaxation (opening of AV value)

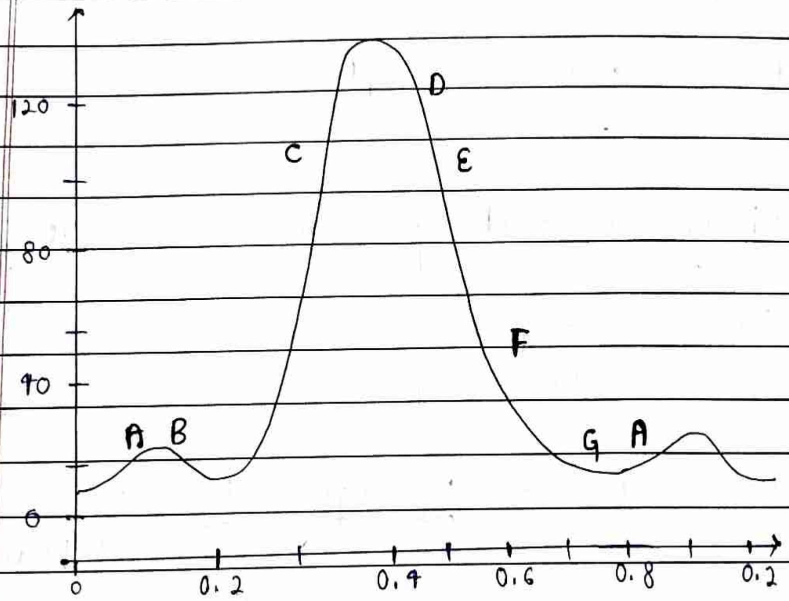
Date
Page

★ Intra ventricular Pr. change during cardiac cycle

↑ **Significance** → Essential for the circulation of blood.

→ **Method of Study** → By cardiac catheterization

→ **Intra ventricular Pr. Curve**



A-B seg. → • atrial systole
• B indicates closure of AV valve.

B-C seg. → • Isometric contraction
• C indicates opening of Semilunar valve.

C-D seg. → • Ejection period
• 1st part of curve → indicates maxm ejection & pr. ↑ses to maxm.
• 2nd part —"— → indicates slow ejection & Pr. ↓ses.

OPPO A53
2022/07/ 5 23:06

OPPO A53
2022/07/15 23:06

* Maxm Pr. of Rt ventricle → 25 mm Hg
* ——"—— Lt. ——"—— → 120 mm Hg
* ——"—— Rt. Atrium → 5 to 6 mm Hg
* ——"—— Lt. Atrium → 7 to 8 mm Hg

D-E seg → • Protodiastole
• E indicates closure of Semilunar valve.

E-F seg → • Isometric Relaxation
• F indicates opening of AV valves.

F-G seg → • Rapid filling phase

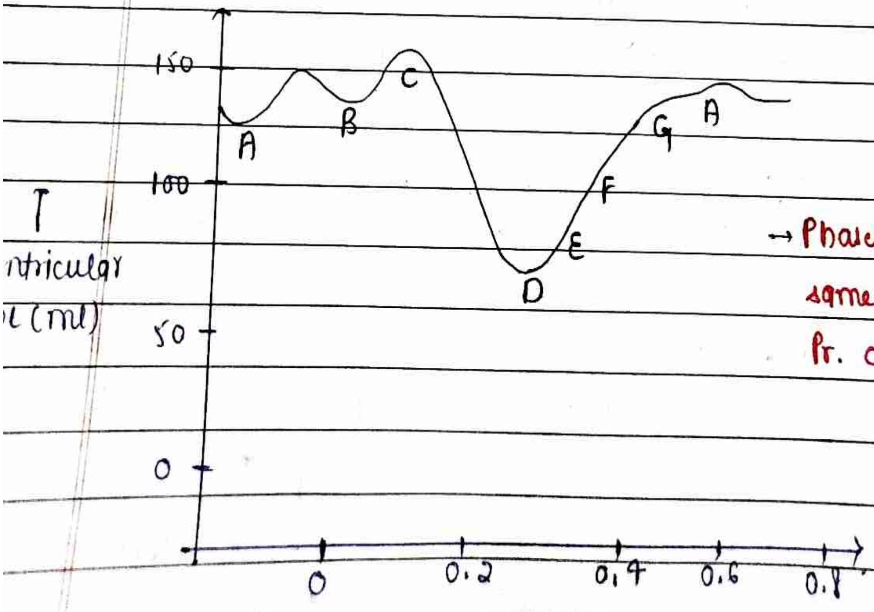
G-A seg → • Slow filling phase

★ Ventricular volume change during cardiac cycle

→ Significance → Imp. to maintain cardiac output & Blood Coagulation.

→ Method of Study → By Angiography → radiographic study of heart & vessels

→ Ventricular volume curve



→ Phases are described same as Intra ventricular Pr. change (वहीं लिखना है)

OPPO A53

Aortic Pr. change during Cardiac cycle

→ **Significance** :- Imp. to maintain blood flow through the circulatory system.

→ **Method of study** :- By catheter

→ **Maxm & minm Pr. in Aorta** :-

→ Pr. is always high then pulmonary Ar.

↓

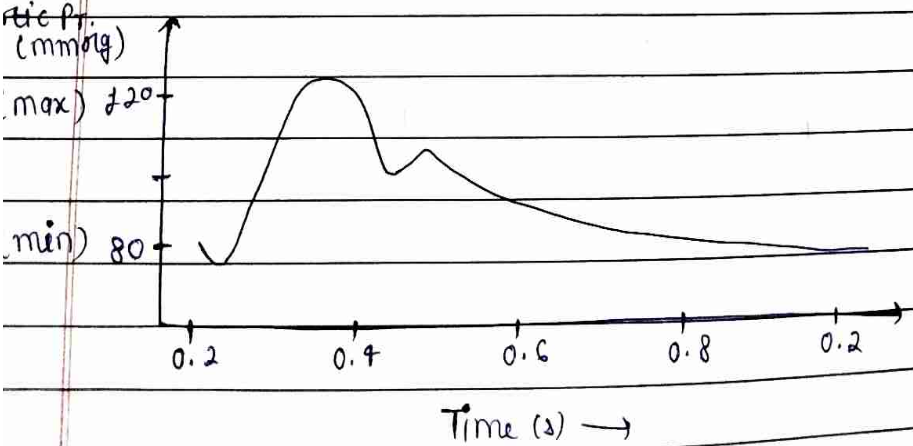
b/c Pr. in Lt. Ventricle > Pr. in Rt. Ventricle
(7 to 8 mmHg) (6 to 7 mmHg)

→ minm pr. is much greater then minm pr. in Lt. ventricle.

↓

b/c of presence of elastic tissue which recoils it

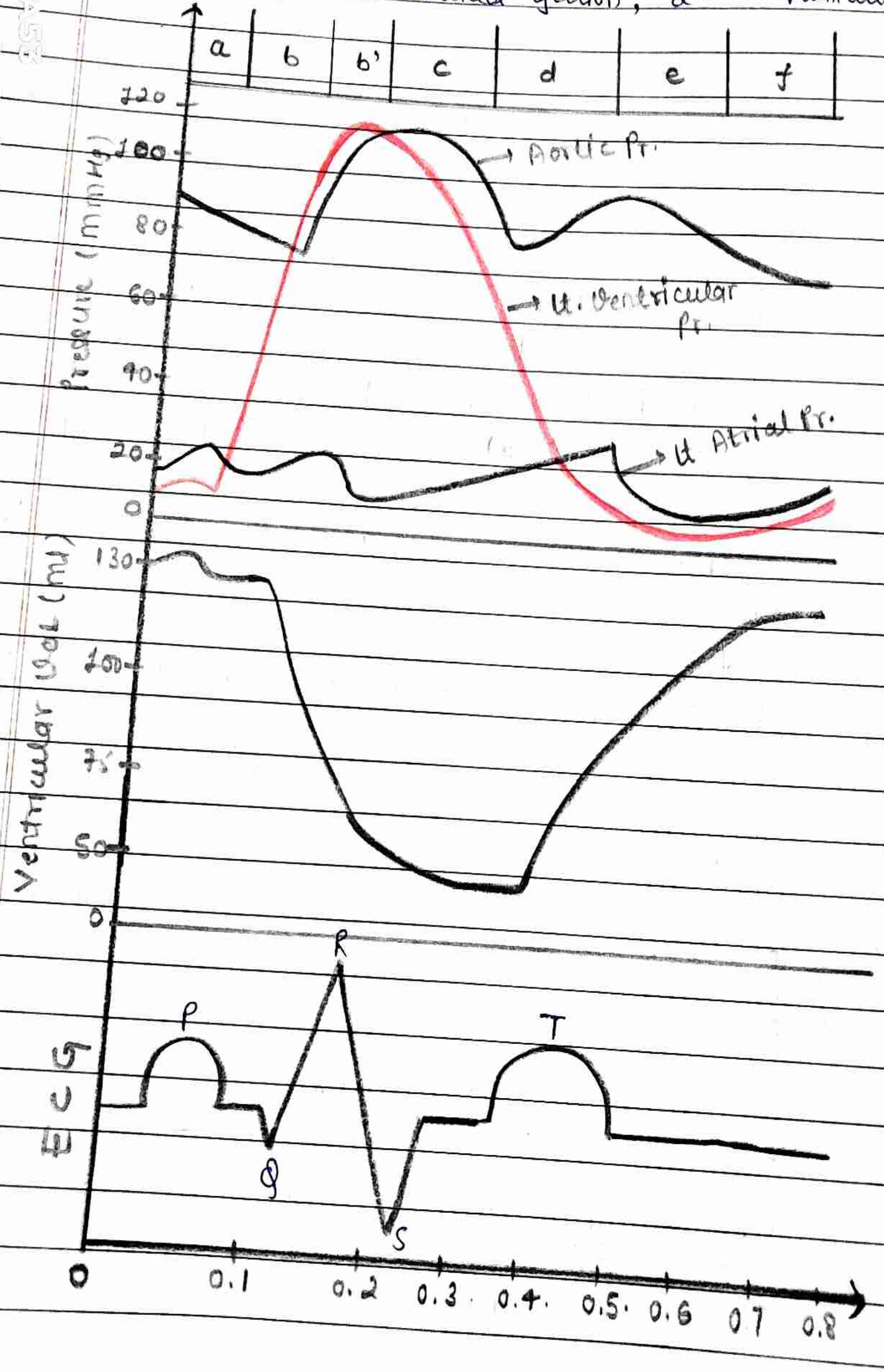
→ **Aortic Pr. Curve**



e = Rapid filling , f = Reduced filling

a ⇒ Atrial Systole , b = Ventricular Isovolumetric Contraction

b' → Rapid Ejection , c = Reduced Ejection , d = -"- Relaxation


a
b
b'
c
d
e
f
120
100
80
60
40
20
0
Pressure (mmHg)
Aortic Pr.
Lt. Ventricular Pr.
Lt Atrial Pr.
130
100
75
50
0
Ventricular Vol (ml)
ECG
P
Q
R
S
T
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8

③ HEART SOUNDS

① 1st Heart Sound

→ Produce during isometric contraction, due to closure of AV valve. & earlier part of ejection Period

★ Cause :- • Sudden & Synchronous closure of AV valve.
• other factors involved are :-

a) Valvular factor → Vibration in the valvular leaflets & chordae tendinea.

b) Vascular factor → Rush of blood into aorta & P. Artery during ejection period.

c) Muscular factor → Myocardial tension & the contraction of ventricular muscles during isometric contraction

d) Artiral factor → Vibration produce by atrial systole

★ Characteristics :- • Long, Soft & low pitched
• Resembles 'LUBB'
• Duration = 0.10 to 0.17 = 0.15 sec
• ν = 25 to 45 c/sec (Hz)
• Concides with the peak of R-wave

★ Applied :-

1. Reduplication → Splitting of 1st HS b/c AV valve do not close simultaneously.

Stenosis → narrowing of a passage

2. Soft 1st H.S. → • Heard in low B.P., Heart failure, MI.

3. Loud / Accentuated 1st H.S. → Heard in condn like mitral stenosis, wolff - parkinson white syndrome.

4. Cannon Sound → • H.S. that is heard intermittently. (रुक - रुक के)
   • Heard in ventricular Tachycardia & Complete AV-block.

② 2nd Heart Sound

→ Produced at the end of protodiastolic period.

★ Cause :- Sudden & Synchronous closure of Semilunar valve

★ Characteristics :- • Short, Sharp & High Pitched.
   • Resembles 'DUBB' (or DUP)
   • Duration = 0.10 to 0.14 sec = 0.12 sec
   • ν = 50 c/sec (Hz)

★ Applied

1. Reduplication → • Asynchronous closure of semilunar valve.
   • Physiological → Pulmonary valve closes little later then aortic valve.
   • Pathological → • pulmonary stenosis,
      • Rt. ventricular hypertrophy
      enlargement of organ due to ↑se in size of its cells

Reverse Splitting / Paradoxical splitting → • Aortic valve closes later
   • Common in Lt. ventricular Hypertrophy, Aortic Stenosis

OPPO A53
2022/07/15 23:07

Date ________
Page ________

2. loud 2nd H.S. → • produced by closure of either Aortic / Pulmonary valve.
- Aortic वाली during Systemic Hypertension
- Pulmonary वाली during Pulmonary —''—

3. Soft 2nd H.S. → Heard in Heart failure

★ Heart Sound & ECG
Coincides with T-wave

③ 3rd Heart Sound (also c/d Ventricular gallop / Protodiastolic gallop)
→ Produced during Rapid filling period
→ Inaudible by Stetho. & Audible by microphone

★ Cause :- Rushing of blood into ventricles
↓
sets up vibration in Ventricular wall & chordae tendinae

★ Characteristic :-
- Short & Low pitched
- Duration = 0.07 to 0.10 sec = 0.1 sec
- ν = 1 to 6 c/sec (Hz)

★ Cond^n when become audible by Stetho
→ Can be heard in Children & Athelete
→ Pathologically → audible during aortic regurgitation, cardiac failure, cardiomyopathy.
↓
(disease of heart muscle)

→ when heard by Stetho c/d Triple H.S.

★ Heard best at
- apex beat area
- patient lie on Lt. side position

OPPO A53
2022/07/15 23:07

★ 3rd H.S. & ECG
Appears b/w T & P waves

④ 4th Heart Sound (also c/d Atrial / Presystolic gallop)
→ Produced during Atrial Systole (late diastole)
→ Inaudible & becomes audible only in pathological condn
→ Studied by graphical recording → Phonocardiography

★ Causes :- • Produced by contraction of Atrial musculator
& vibrations set up in Atrial musculator.

★ Characteristics :- • Short & Low pitched
• Duration = 0.02 to 0.04 sec = 0.03 sec
• ν = 1 to 4 c/sec (Hz)

★ Condn when becomes audible
→ Audible by stetho. when ventricles becomes stiff
↓
b/c atria contract forcefully to overcome the stiffness

→ Audible during → Ventricular hypertrophy, Aortic Stenosis
→ When heard by stetho → Triple H.S.
→ Heard best at :- • apex ~~beat~~ area
• Patient lie in supine position

Method of Study of H.S.

1. By stetho → 1st H.S. (at Mitral & Tricuspid area)
2nd H.S. (at Pulmonary & Aortic area)
2. By microphone → 1st, 2nd & 3rd
3. By Phonocardiogram → 1st, 2nd, 3rd & 4th by using
↓
electronic sound transducer

④ ELECTROCADIOGRAM (ECG)

→ Defined as the graphical record of electrical activity of the heart obtained by placing electrodes on the surface of the body that records the voltage difference generated by the heart.

→ Electrocardiograph → is the instrument by which electrical activities of heart are recorded.

★ Uses of ECG

→ Used in determining & diagnosing the following :-

1. Heart rate
2. Heart rhythm
3. Abnorml Electrical conduction
4. Poor blood flow to heart muscle (Ischemia)
5. Heart Attack
6. Hypertrophy of chambers
7. CAD

★ ECG Leads

→ ECG is recorded by placing series of electrodes on surface of body.

→ Electrodes are c/d ECG leads & connected to ECG machine
↓
fixed on limbs (Rt. arm, Lt. arm & Lt. leg are chosen).

→ Heart is said to be in centre of an imaginary equilateral Δ, c/d Einthoven Δ.
↓
drawn by connecting roots of these 3 limbs

OPPO A53
2022/07/15 23:07

Date ______
Page ______

Imp. ☆ **Bipolar limb leads**

→ also k/n as Standard limb leads.

→ 2 limbs are connected to obtain these leads & both the electrodes are Active Recording Electrodes
↓
one is (+) & other is (-)

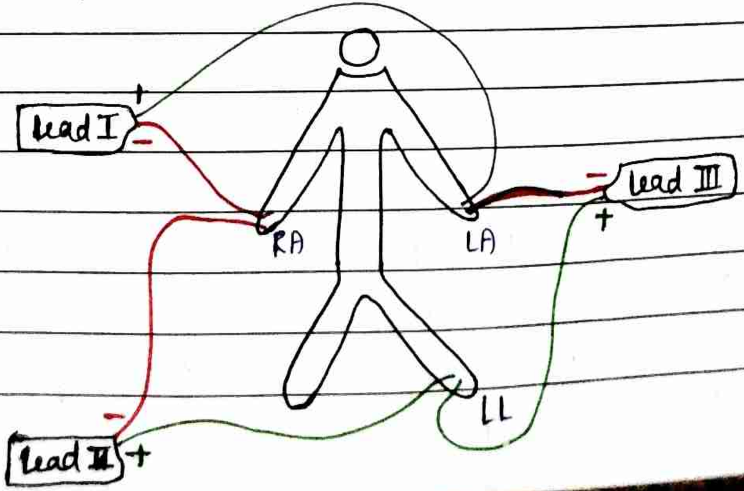
→ Electrode applied to Rt. leg acts as a ground wire
↓
(prevents ext. disturbance)

→ There are of 3 types :-

1. Limb lead - I
→ obtained by connecting Rt. arm & Lt. arm.
→ Rt. → to (-)ve terminal
Lt. → to (+)ve terminal

★2. Lead - II
→ obtained by connecting Rt. arm & Lt. leg.
→ Rt arm → to (-)ve terminal
→ Lt. leg → to (+)ve terminal

3. Lead - III
→ obtained by connecting Lt. arm & Lt. leg
→ Lt. arm → to (-)ve terminal
→ Lt leg → to (+)ve terminal



OPPO A53
2022/07/15 23:07

★ **Normal ECG**

ECG tracing shows diffn waves, segments & Intervals as depicted from lead II tracing.

① ECG Waves

i) P-wave → • 1st positive deflection
- produced due to atrial depolarization
- Duration = 0.1 s

ii) QRS complex → • Consist of :- Q wave → small (-) ve
R wave → (+) ve
S wave → small (-) ve
- produced due to ventricular depolarization
- Duration = 0.08 to 0.1 sec

iii) T wave → • (+) ve deflection
- produced due to ventricular repolarisation
- Duration = 0.2 sec

iv) U wave → • final (+) ve deflection
- not always seen & is insignificant
- Supposed to be due to repolarisation of papillary muscles / purkinje fibres

② ECG Segments

i) PR segment → • lies b/w end of P-wave & start of QRS complex.

i) ST segment → • lies b/w end of QRS complex & start of T-wave.

OPPO A53
2022/07/ 15:23:07

* J-point → point where QRS complex ends & ST seg. begins

③ ECG Intervals

→ Includes waves & segments

i) PR Interval →
- Interval b/w the onset of P-wave & onset of QRS complex.
- Duration = 0.12 to 0.2 sec
- Represents atrial depolarisation & conduction through AV node.

ii) QRS Interval →
- Interval measured from onset of Q-wave to the J-point.
- Duration = 0.08 to 0.1 sec.

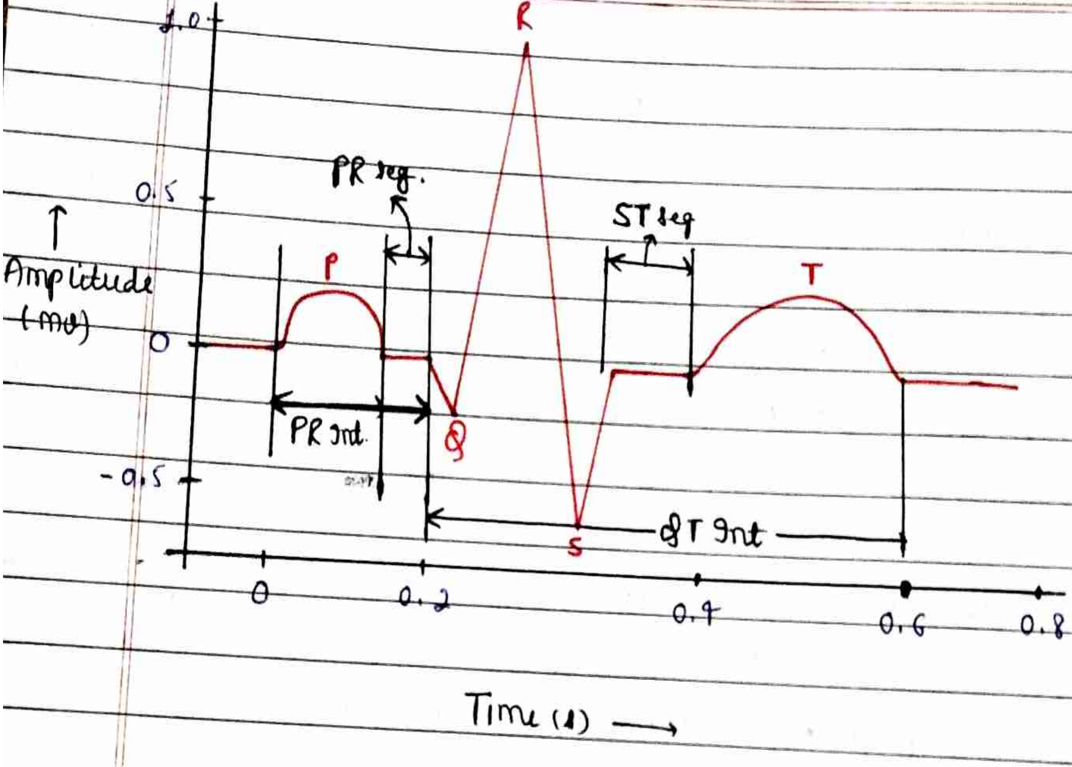
↓ Represents ventricular depolarisation & Repolarisation.

iii) ST Interval →
- Interval b/w J-point & end of T-wave
- Duration = 0.32 sec
- Represents ventricular repolarisation

iv) PP Interval →
- Interval b/w either the peak / beginning of 2 successive P-waves.
- Measured for calculation of Atrial Rate

v) RR Interval →
- Interval b/w 2 successive R waves
- Measured for calculation of Heart Beat/Rate.

OPPO A53
2022/07


1.0
0.5
0
-0.5
Amplitude (mV)
P
PR seg.
PR Int.
Q
R
S
ST seg
T
QT Int
0
0.2
0.4
0.6
0.8
Time (s)

OPPO A53
2022/07/15 23:08

⑤ CARDIAC OUTPUT

→ Amount of Blood ejected by each ventricle per minute.

$$\boxed{\text{Cardiac output} = \text{Stroke Vol.} \times \text{Heart Rate}}$$

* Nrml value :- 5-6 L/min (8% of body wt.)

→ **Stroke Volume**

- defeined as the volume of blood ejected by each ventricle with each beat.

*Nrml value :- 70 ml (60 to 80ml) when heart rate is nrml (72/min).

→ **Cardiac Index**

- Cardiac output per sq. meter of body surface area.
- calculated by dividing C.O. at rest with body surface area in m^2.

$$C.I. = \frac{C.O.}{S.A.(m^2)} \Rightarrow \frac{5\ L/min}{1.7\ m^2}$$

$$C.I. = 3\ L/min/m^2$$

*Nrml value :- 3.2 L/min/m^2

Significance → Standardize C.O. among individuals of diffⁿ body sizes.

Effect of Age → ↓ses with age due to ↓sed activity & declining muscle mass with age.

OPPO A53
2022/07/15 23:08

→ Cardiac Reserve

amount of blood that can be pumped by each ventricle in excess of nrml C.O.

*Nrml value :- 15-25 L/min (non-athletes)
20-40 L/min (athletes)

→ End diastolic, End systolic & Ejection fraction → already done

* Factors Affecting Cardiac Output

① Factors affecting stroke volume
→ depends on 3 major factors

i) Preload
→ Stretching of cardiac muscles fibres at the end of diastole
→ just before contraction.
→ Due to ↑se in ventricular pr. caused by filling of blood during diastole.
→ Stretching of muscle fibres ↑ses their length
↓
causes ↑se in force of contraction & C.O.

End diastolic filling (EDF) → preload of ventricle
End diastolic volume (EDV) → measure of preload.

→ This is explained by Frank starling law of Heart

OPPO A53
2022/07 18

Imp. ★ **Frank Starling's Law**

→ Force of contraction ∝ Initial length of muscle fibre (within the physiological limit)

→ This explains how the ↑se in length preload or EDV ↑ses C.O.

→ Initial length ⇒ length of muscle fiber prior the ventricular contraction (i.e. just before the onset of systole).

↓

depends on level of stretch of ventricular muscles at the end of diastole.

↓

depends on degree of ~~filling of~~ End diastolic filling

↓

↑sed filling ↑ses the fibre length

↓

that ↑ses force of contraction

→ Also k/n as Heterometric-Autoregulation of C.O.

★ **Factors affecting Preload**

→ End diastolic filling of ventricle depends on 3 major factors :-

1. Venous Return
2. Atrial Pump Activity
3. Ventricular Compliance

OPPO A53
2022/07/15 23:08

Imp.* 1. **Venous Return**

→ Amount of blood that returns to Rt. atrium from systemic venous circulation.

→ Depends on many factors such as :-

i) Skeletal muscle pump

→ In lower limb, contraction of skeletal muscles compresses the veins & pushes blood towards heart & backflow is prevented by closed distal valves.

↓

This ↑ses the venous return.

→ C.O. ↑ses by ↑sed skeletal muscle activities (Ex:- walking)

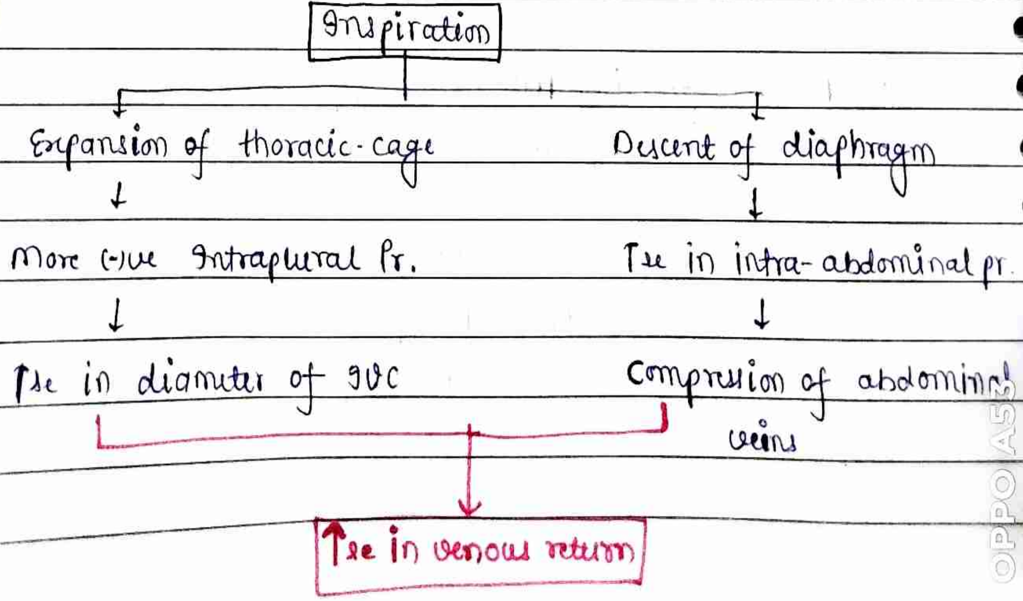
→ During quiet standing for long time, pooling of blood occurs in veins due to absence of muscle activity.

↓

↓ses the venous return & C.O.

ii) Thoracic Pump & Abdominal Pump

→ Venous return ↑sed during inspiration


Inspiration
Expansion of thoracic-cage
Descent of diaphragm
More (-)ve Intrapleural Pr.
↑se in intra-abdominal pr.
↑se in diameter of IVC
Compression of abdominal veins
↑se in venous return

OPPO A53
2022/07/15 23:08

iii) ECF volume

→ ↓se in ECF vol. ⇒ ↓se in C.O. [Diarrhea, vomiting]

→ ↑se in ECF vol. ⇒ ↑se in C.O. [Pregnancy]

iv) Sympathetic Activity

→ Veins are innervated by sympathetic fibres

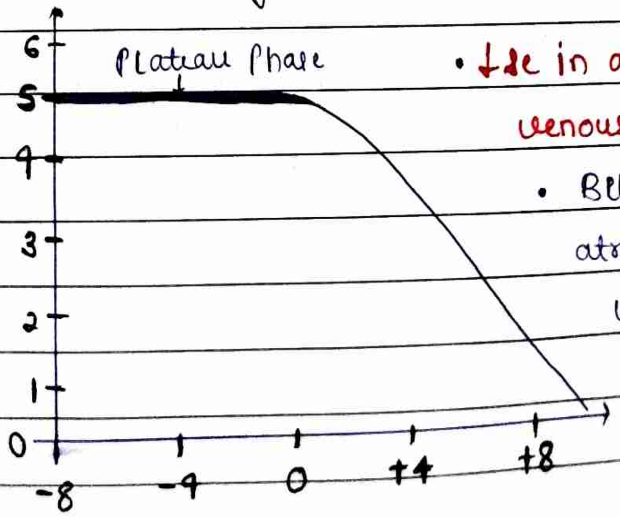
Sympathetic System

Stimulation	↓sed stimulation
↓	↓
Venoconstriction	Vasodilation
↓	↓
↑se venous return	↓se venous return
↓	↓
mechanism to ↑ses C.O. during exercise	due to pooling of blood

v) Rt. Atrial Pr.

→ It exerts a backward force on veins to impede flow of blood from the veins into Rt atrium.

→ Effect is depicted by venous return curve



- ↓se in atrial Pr, ↑se in venous return
  - Below -2mmHg Rt. atrium cannot ↑se venous return (Plateau)
  - Become almost zero above 7mm Hg

vi) Degree of filling of Systemic Circulation

→ It forces the systemic blood towards the heart.

vii) Resistance to venous return

→ Resistance to flow of blood b/w peripheral vessels and Rt. atrium, c/d Venous Resistance.

→ Imp. in determining venous return, b/c when venous resistance ↑ses, blood begans to dammed up in venous compartment.

→ Rise in venous pr. is not effective in overcoming the resistance

↓

b/c veins are highly distensible

→ Even slight accumulation of blood in arteries raises the pr. greatly

↓

b/c they have less capacitance

↓

So, High Pr. in Ar. overcome much of the resistance

Resistance to Venous return is determined by

2/3rd by venous resistance

1/3rd by arteriolar & small artery resistance

OPPO A53
2022/07/15 23:08

2. **Atrial Pump Activity** → • ventricular filling occurs mostly passively
• About 15-20% filling at rest occurs due to atrial contraction
↓
(atrial pump activity)

3. **Ventricular Compliance** → • Nrmlly, ventricular muscles is stretchable (compliant) enough to accomodate adquate blood during diastole [Nrml EDV = 130 ml].
• filling ↓sed in cardiomyopathies due to ↓sed compliance

ii) Myocardial Contractility (M.C.)

→ Exerts a major influence on C.O.
→ Factor that ↑ses M.C. → positively inotropic
↓se M.C. → negatively inotropic

→ It depends on :-
1. Ventricular muscle mass
2. State of autonomic activity
3. conc. of various hr. & chemicals in body / blood
4. Drugs
5. Heart rate

iii) Afterload

→ Force against which ventricles must contracts & eject the blood.
→ It is the resistance offered against ejection of blood from ventricle.
→ At the end of isometric contraction, semilunar valves are opened & blood is ejected into aorta & pulmonary

OPPO A53
2022/07/15 23:08

artery. So, the Pr. ↑ses in these 2 vessels

↓

Now, ventricles have to work against this pr. for further ejection

→ $C.O. \propto \frac{1}{\text{Afterload}}$ ↑se in peripheral resistance, ↓ C.O. & vice versa

* Peripheral Resistance is considered as afterload

② Factors affecting Heart Rate

→ Influenced mainly by Autonomic Activity

→ Vagal Stimulation → ↓ses heart rate

Sympathetic Stimulation → ↑ses heart rate

* Unless associated with ↑sed venous return (EDV), ↑se in H.R. may not ↑se cardiac output.

→ In tachycardia → duration of diastole shortens then systole

↓

ventricles gets less time to filled

↓

thus, EDV ↓ses

↓

∴ C.O. does not ↑ses proportionately to that of ↑se in H.R.

Similarly, when H.R. ↓ses diastolic filling of ventricles ↑

↓

Compensate to maintain C.O.

OPPO A53

★ Measurement of Cardiac Output

1. Direct Methods

→ C.O. is measured directly by placing an electromagnetic flow meter in ascending aorta or by using cardiometer.

→ These methods are applied only in experimental animals or in humans (in patients)

→ In humans, C.O. is determined by using Dopplers combine with Echocardiography.

2. Indirect Methods

1. Ficks method
2. Indicator dilution method
3. Thermo dilution method
4. Ballistocardiography
5. Echocardiography
6. X-ray method
7. Pulse pr. method

Imp. → Ficks Method

Ficks Principle → defined as the amount of a sub. taken up by an organ or by the whole body per unit of time or given out in a unit of time is the product of amount of blood flowing through the organ & the arteriovenous diffⁿ of the sub. across the organ.

Amount of sub. taken/given ⇒ Amount of blood flow/min × Arteriovenous diffⁿ

OPPO A53

★ **Procedure :-** C.O. can be measured by measuring the amount of O_2 consumed by the body in a given period & dividing this by arteriovenous diffⁿ of O_2 across lungs.

1. O_2 consumption measured by Spirometer
2. Arterial content of O_2 measured by blood from any peripheral ar. = 20 ml/ 100 ml of blood
3. Venous blood is collected from pulmonary Ar. = 15 ml/ 100 ml of blood

$$C.O. = \frac{O_2 \text{ consumption } (ml/min)}{(AO_2) - (VO_2)}$$

$$= \frac{250}{\frac{20}{100} - \frac{15}{100}} = \frac{250}{5/100} = 5000 \text{ ml/min}$$

$$= 5 \text{ L/min}$$

★ Advantages

1. Result is accurate
2. No chemical is injected

★ Disadvantages

1. It is difficult to measure C.O. by this method in abulatory patient & during exercise.
2. Catheterization should be done by expert hand.

OPPO A53
2022/07/15 23:23

Date ______
Page ______

⑥ HEART RATE

→ Nrml H.R. is 60-100 beats / min

→ H.R. less then 60 beats / min → Bradycardia

H.R. greater then 100 beats / min → Tachycardia

→ Nrmlly more in Infants & Childrens.

→ H.R. reflects the rate of discharge of Cardiac pacemaker.

↓

* H.R. is the rate of discharge of SA node

★ Variation in H.R.

→ Causes of Tachycardia

Physiological → Exercise, After Eating, Anger, Emotion, Infants, Pregnancy, High environmental temp

Pathological → Fever, Anemia, Heart failure, AV fistula, Hyperthyrodism

→ Causes of Bradycardia

Physiological → Sleep, Athelets, Fear, old age, yogis

Pathological → ↑ed Intracranial Pr., Heart attack, obstructive jaundice, Hypothyrodism

★ Regulation of H.R.

→ H.R. is primarily a vagal function

→ Mechanism divided into 2 categories :-

OPPO A53
2022/07 15:23:24

Date
Page

1. Neuronal Control Mechanism

→ 2 categories :-

i) Autonomic Control

→ Nrmlly P.S. control dominates the S control.

∴ Basal H.R. is always < Intrinsic H.R.

↓

Rate of discharge of SA node when the heart is completely denervated. It is about 110 / min

Parasympathetic Control (P.S.)

→ P.S. fibres arises in nucleus tractus solitarius (NTS) in medulla.

→ Rt vagus N. → supplies SA node

Lt. vagus N. → supplies AV node

→ Stimulation of vagus N. ↓ses H.R.

↓

- due to secretion of Acetylcholine

→ Effect of vagus N. remains for short period as acetylcholine is rapidly hydrolysed by cholinesterase.

Sympathetic Control (S) → fibres arise from lower 2 Cervical & upper 6 thoracic seg. of spinal cord.

→ Stimulation of S fibres ↑ses H.R.

→ Effect of S stimulation persist longer as there is no enzyme for degradation of norepinephrine

OPPO A53
2022

Date
Page

ii) Reflex Control

→ Reflexes that regulates B.P. also control H.R.

- Baroreceptor Reflex → • Receptors located in Carotid sinus & Aortic Arch
  • stimulated when BP rises, which stimulates NTS
  ↓
  NTS stimulates vagus N. that causes Bradycardia.

- Chemoreceptor Reflex → • Stimulated by change in chemical composition of blood as in Hypoxia, Hypercapnia & acidosis
  • Activation produces Bradycardia

** Bainbridge Reflex → In dogs, rapid infusion of saline / blood, ↑ses H.R. if the initial H.R. is less.

→ Receptors are ⊕nt in atria & at Veno-atrial junction Hn as tachycardia producing receptors (TBR)

→ Reflex accounts for tachycardia.

→ Effect of reflex is more observable if initial H.R. is less.

→ This reflex compensates with Baroreceptor reflex & ↑ses H.R. & Abolish following vagotomy as mediated by vagus N.

- Cushing Reflex → • Activated in Hypovolmia & Hypotension that ↓ses Blood flow to vasomotor center (VMC)
  ↓
  that produces vasoconstriction & tachycardia
  • But the consequent ↑se in BP activates baroreceptor & results in bradycardia.

OPPO A53
2022/07/15 23:24

2. Humoral Control Mechanism

i) Hormonal Control → Thyroxine & Catecholamines ↑ses H.R.

ii) Chemical control → Hypoxia ↑ses H.R.
↓
mediated by release of catecholamines from adrenal medulla

★ Effect of Exercise on H.R.

→ H.R. ↑ses during exercise b/c of impulse from cerebral cortex to medullary centers, which reduces vagal tone

→ In moderate Exercise ⇒ H.R. ↑ses to 180 beats/ min

In severe muscular Exercise ⇒ H.R. reaches to 240 beats/ min

→ ↑ed H.R. is mainly due to ↓ses vagal tone / vagal withdrawal

→ ↑ed H.R. is b/c of following factors :-

1. Impulses from proprioceptors → act through higher centers
2. ↑ed CO_2 tension → act through medullary centers
3. ↑ed body temp → acts on cardiac centers through Hypo-thalamus
4. Circulating catecholamines → secreted during exercise

OPPO A53
2022/07/ 5 23:24

⑦ BLOOD PRESSURE

→ Defined as the lateral pr. exerted by the column of blood on the wall of Arteries.

→ B.P means the Arterial Pressure

→ fluctuates during systole & diastole of heart.

★ Systolic Blood Pr.

→ Maxm pr. recorded during systole of heart.

→ Nrml value = 100 - 119 mm Hg (120 mm Hg)

→ depends mainly on C.O. [SBP ∝ C.O.]

★ Diastolic Blood Pr.

→ Minm pr. recorded during diastole of heart

→ Nrml value = 60-79 mm Hg [80 mm Hg]

★ Pulse Pr. (PP)

→ Diffn b/w Systolic & diastolic B.P.

→ Nrml value = 20-50 mm Hg (70 mm Hg)

★ Mean Arterial Blood Pr. (MAP)

→ Average Pr. recorded during the cardiac cycle.

→ As the duration of systole is less then the duration of diastole, the MAP is less then the value halfway b/w systolic & diastolic pr.

$$\text{MAP} = \text{Diastolic Pr.} + \frac{1}{3}\text{ P.P.}$$

$$= 80 + \frac{40}{3} = 93.3 \text{ mm Hg}$$

Nrml value = 75-105 mm Hg

OPPO A53
2022/07/15 23:24

Significance :- • Helps in forward movement of blood in lumen of Blood vessels
• also maintains perfusion of tissues

200*

Regulation of Blood Pr.

① Short Term Regulation of B.P.

→ Regulation of BP within seconds to minutes

→ Occurs mainly by neural mechanism, vascular & Hormonal mechanisms also contribute

→ Mechanisms are as follows

i) Neural Mechanism

- Autonomic Regulation → Sympathetic
  - → Parasympathetic
- Medullary control
- Hypothalamic Control
- Cortical control
- Reflex Regulation → Baroreceptor
  - → Chemoreceptor
  - → Cushing reflex
  - → Somatosympathetic
  - → Arterial Stretch
  - → Ventricular & Pulmonary Stretch
  - → Coronary & Pulmonary Chemoreflexes
  - → Bainbridge reflex

ii) Vascular Mechanism

- Capillary fluid shift
- Stress Relaxation

OPPO A53

iii) Hormonal ~~Relaxation~~ Mechanism

- Catecholamines
- Renin-Angiotensin System
- ADH
- ANP
- Kinin Kallikrein System
- Histamin
- Endothelins
- Endothelium derived relaxing factor (EDRF)
- Adrenomedullin

1. Neural Mechanism

- Autonomic Regulation

→ mainly by Sympathetic control as systemic blood vessels are innervated by S. fibres & they lack P.S. innervation.

→ Sympathetic Control
- main control mechanism
- 2 types of sympathetic system are :-

★ Sympathetic Vasoconstrictor System

→ Non-adrenergic fibres suppling blood vessels are vasoconstrictor in nature.

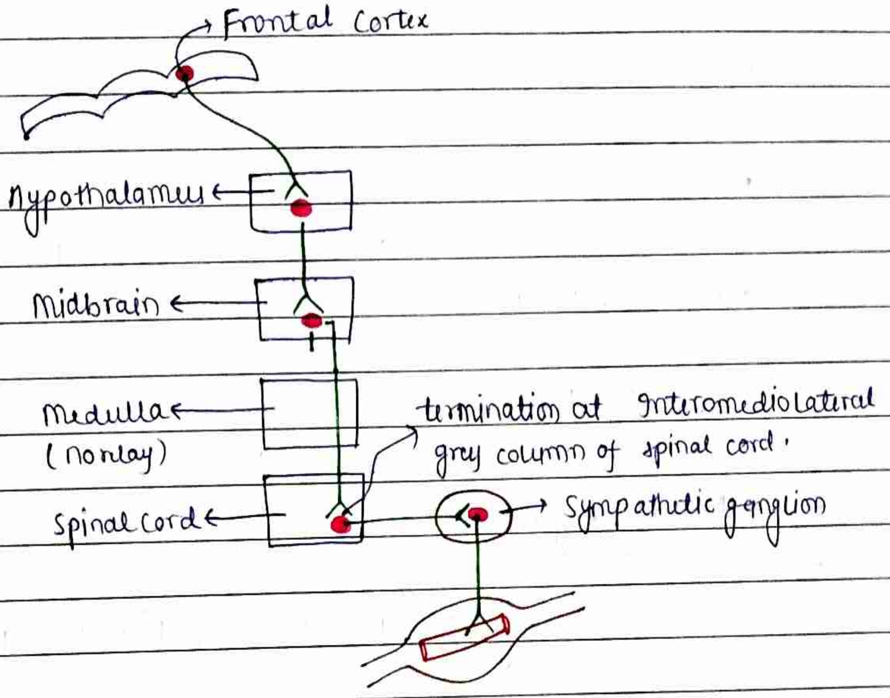
∴ stimulation of these fibres ↑ses B.P.

→ Sympathetic stimulation ↑ses B.P. by following mechanism :-
- Vasoconstriction
- Venoconstriction
- Cardiac Stimulation
- ↑ed secretion of Catecholamines

OPPO A53
2022/07/15 23:24

Sympathetic Vasodialator System

→ fibres supplying arteries & arterioles of skeletal muscle produce vasodilation as innervated by **Sympathetic cholinergic fibres**.


Frontal Cortex
Hypothalamus
Midbrain
Medulla (no relay)
Spinal cord
termination at Interomediolateral grey column of spinal cord.
Sympathetic ganglion

→ There is no basal tonic discharge of sympathetic vasodilator fibres

→ Parasympathetic Control

- Systemic Blood vessels = not supplied by parasympathetic fibres
- However, vagal stimulation = ↓se B.P. by ↓sing H.R. & C.O.

- Medullary Control

→ Cardiovascular centres mainly located in ~~Hypothalamus~~. Medulla

→ primarily control the autonomic output of heart & blood vessels, which is major cardiovascular regulatory pathway

→ They are broadly divided into 2 :-

Vasomotor Center (VMC) → cause intense vasoconstriction &

OPPO A53
2022/07 15 23:24

cardioacceleration that ↑ses Blood Pr.

Cardioinhibitory center → causes Bradycardia & ↓ses C.O., Vasodilation & ↓sed B.P.

- **Hypothalamic Control**

→ Stimulation of ant. hypothalamus → Hypotension & Brady-cardia.

—— " —— Posterolateral hypothalamus → Hypertension & Tachycardia

- **Cortical Control**

→ does not directly influence B.P.

→ Motor & premotor cortices stimulation ↑ses B.P.

- **Reflex Regulation of Blood Pr.**

→ Most imp. short - term mechanism as reflexes operate swiftly & effectively.

1. Imp ★ **Baroreceptor Reflex**

→ Most imp as regulates B.P. within seconds.

→ Life saving reflex ~~and~~ also c/d Baroreflex / Sinoaortic Reflex

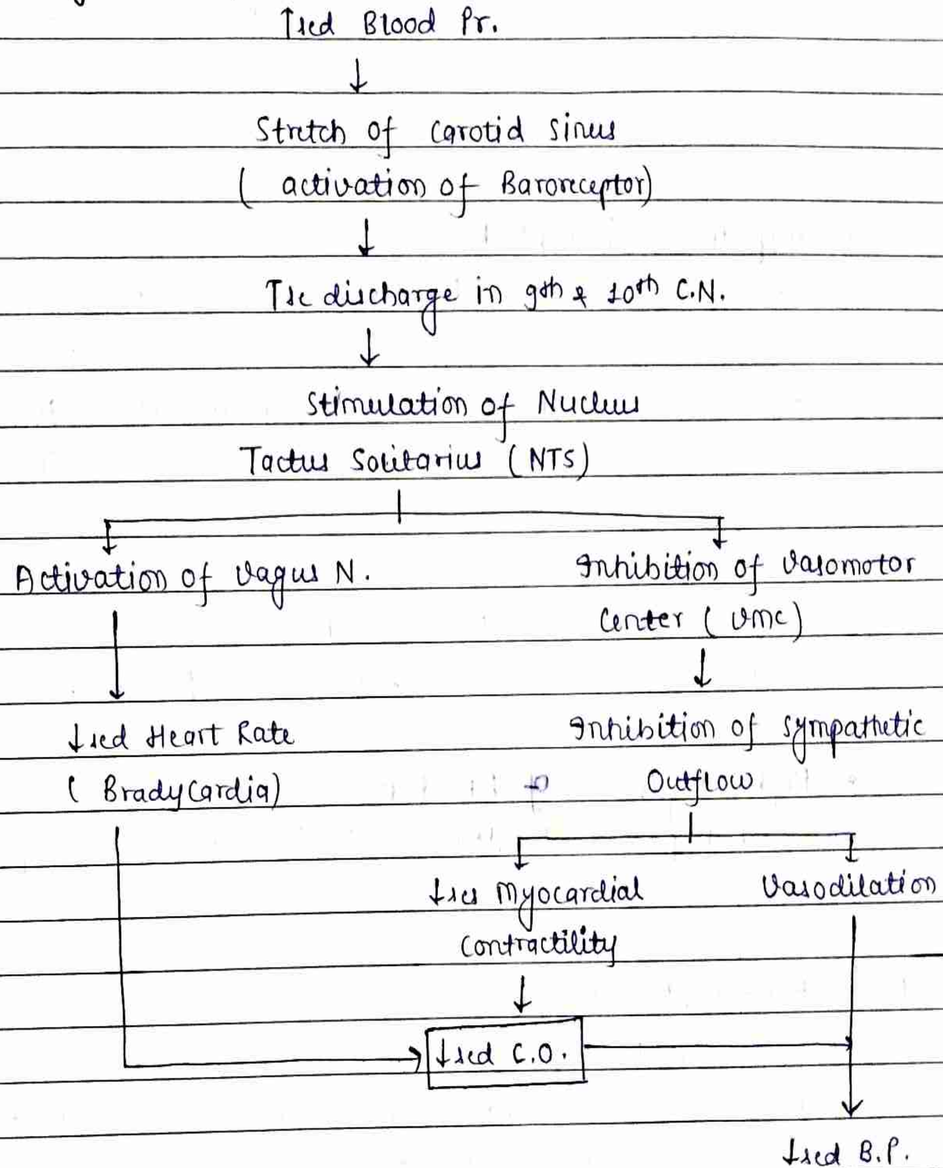
→ Receptors of baroreceptor reflex are High - Pressure baroreceptor that are ⊕nt in wall of Carotid Sinus & Aortic arch.

→ Baroreceptor detect the change in pr. in blood vessels in the wall of which they are located

OPPO A53
2022/07 5 23:24

Date
Page

→ Role of Broreceptors when BP ↑ses


↑ed Blood Pr.
↓
Stretch of carotid sinus
(activation of Baroreceptor)
↓
↑se discharge in 9th & 10th C.N.
↓
Stimulation of Nucleus
Tractus Solitarius (NTS)

Activation of Vagus N.
↓
↓ed Heart Rate
(BradyCardia)

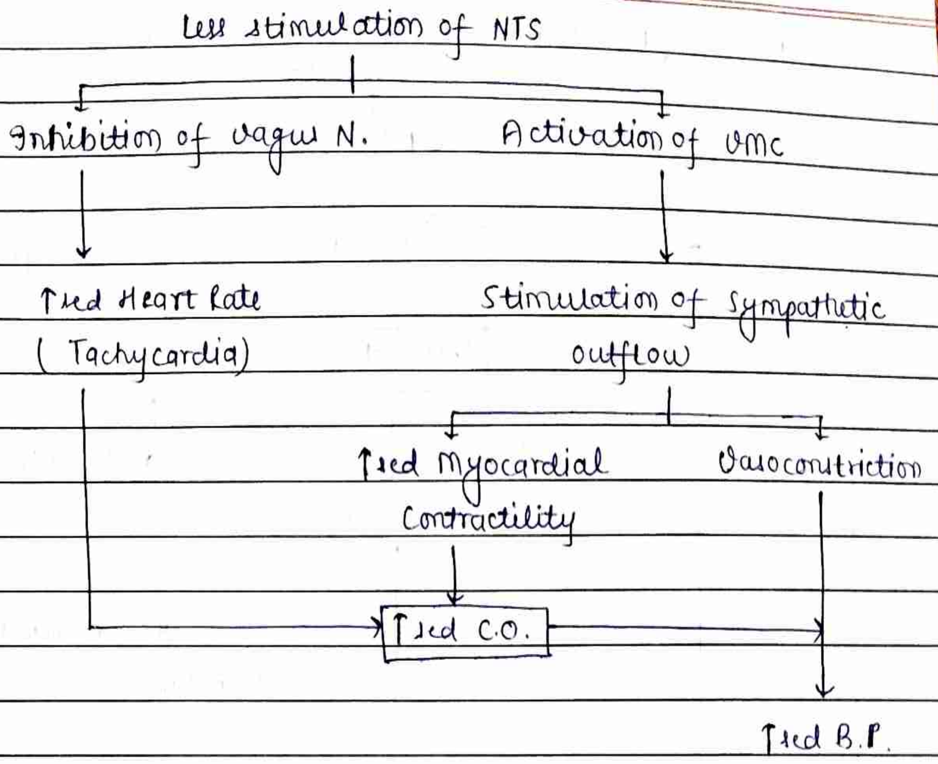
Inhibition of Vasomotor
Center (VMC)
↓
Inhibition of sympathetic
Outflow

↓ses Myocardial
Contractility
↓
↓ed C.O.

Vasodilation

↓ed B.P.

→ Role of Baroreceptor when BP ↓ses
↓ed Blood Pr.
↓
less stretch of carotid sinus
(less activation of Baroreceptors)
↓
↓se discharge in 9th & 10th C.N.
↓


Less stimulation of NTS
Inhibition of vagus N.
Activation of VMC
↑ed Heart Rate (Tachycardia)
Stimulation of Sympathetic outflow
↑ed Myocardial Contractility
Vasoconstriction
↑ed C.O.
↑ed B.P.

★ Physiological Significance

1. Operates within few seconds & are 1st & foremost reflex for regulation of BP.

2. Regulates BP over a wide range of fluctuation in Pr. i.e., 50-200 mm Hg.

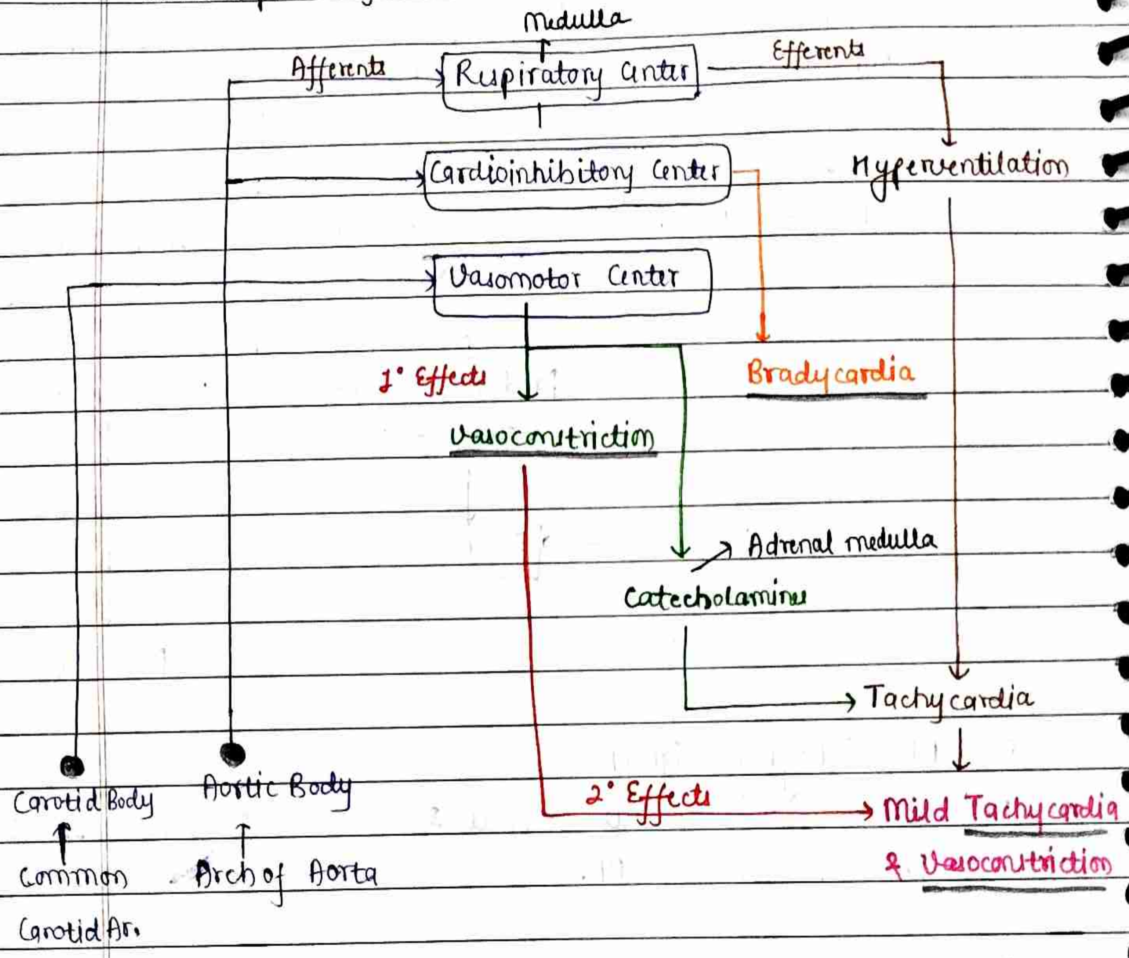
3. Explains the physiological basis of Marey's law which states that $H.R. \propto \frac{1}{B.P.}$ (not vice versa)

4. Baroreceptor resetting occurs in chronic Hypertension.

OPPO A53
2022/07/1 23:25

Date ______
Page ______

2. Chemoreceptor Reflex


Medulla
Afferents
Respiratory Center
Efferents
Cardioinhibitory Center
Hyperventilation
Vasomotor Center
1° Effects
Bradycardia
Vasoconstriction
Adrenal medulla
Catecholamines
Tachycardia
Carotid Body
Aortic Body
2° Effects
Mild Tachycardia
& Vasoconstriction
Common
Carotid Ar.
Arch of Aorta

Afferents from Carotid Body & Aortic Body in 9th & 10th C.N.

↓

→ Stimulates • CIC to produce Bradycardia
• VMC to produce Vasoconstriction } 1° Effects

→ Hyperventilation produced by stimulation of Respiratory Center & Catecholamines secretion of medulla causes ⇒ Tachycardia

↓

Net Effect ⇒ Tachycardia & Vasoconstriction

↓

2° Effect

OPPO A53
2022/07

3. Cushing Reflex / CNS Ischemic Response

Gross Hypotension of ↑sed Intra-cranial Pr.

↓

↓sed cerebral Blood flow / ↓sed Blood flow to VMC

↓

* operates when B.P. falls below 90 mm Hg

Hypoxia & Hypercapnia at VMC

↓

Strong stimulation of VMC

↓

Intense Vasoconstriction

↓

↑sed B.P. in carotid Sinus

↓

Activation of Baroreceptor reflex

↓

Causes Reflex Bradycardia

2. Vascular Mechanism

* Capillary fluid Shift → When B.P. ↓ses (Hemorrhagic shock)

↓

Hydrostatic Pr. in capillaries ↓ses

↓

Shift of fluid from interstitial tissue space ⟶ intravascular compartment through capillary membrane

↓

This is capillary fluid shift

by this ↓

About 300 ml of fluid is added to blood

OPPO A53

★ **Stress Relaxation**

- when BP ↑ses abruptly

↓

Blood vessels distend

↓

Caused active stretch on vessel wall

↓

Smooth muscles of vessels relax in response to stretch

↓

∴ ↓ses Vascular tone & B.P.

3. **Hormonal Mechanism**

→ change BP by causing either vasodilation / vasoconstriction

Vasoconstrictors :- 1. Catecholamines
2. Renin - Angiotensin System (Angiotensin II)
3. Vasopressin
4. Endothelins

↓

↑ses BP

Vasodilators :- 1. ANP
2. Kallikrein - Kinin System (Bradykinin)
3. Histamine
4. Endothelium derived relaxing factor (Nitric oxide)
5. Adrenomedulin

↓

↓ses BP

OPPO A53
2022/07

② Long-Term Regulation of BP

- → Occurs by Renal & Hormonal mechanism
- → Involve change in fluid volume of body.

1. Renal Mechanism

- → Control blood volume by controlling urinary excretion of salt & water.
- → Kidney control blood volume & Pr. by altering 2 primary processes.

[Intrinsic Properties of Kidney to control Blood Vol. & Pr.]

Pressure Diuresis & Pressure Natriuresis

- → with ↑se in arterial BP from 60 to 200 mm Hg

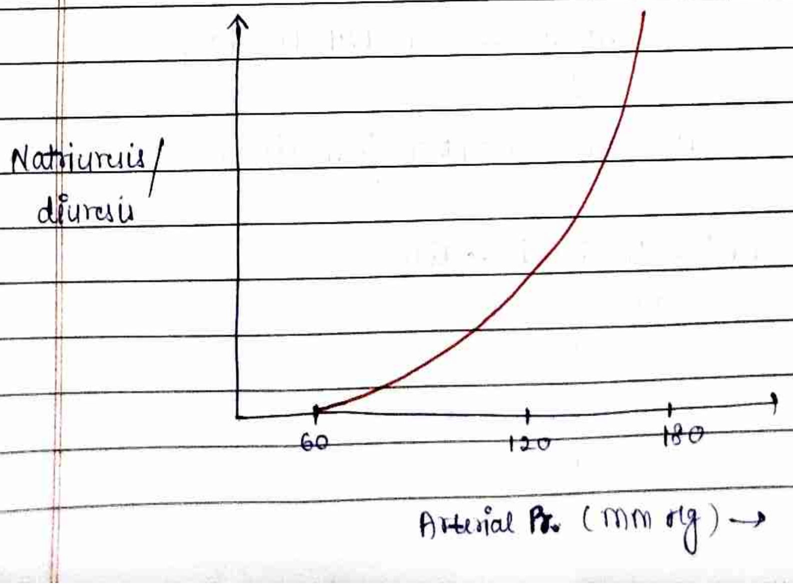
↓

there is progressive ↑se in water excretion (Pr. diuresis) & sodium Excretion (Pr. Natriuresis) in urine

- → Curve b/w arterial Pr. & Urinary Excretion is c/d Renal Output Curve.

↓

less steep from 60-120 mmHg & more from 120 to 200 mmHg



2. Hormonal Mechanism

→ Hr. involved are Aldosterone, ADH & ANP

↓

acts on kidney to regulate Na^+ & water excretion

→ Renin - Angiotensinogen - Aldosterone System

Fall in blood Pr.

↓

Release of Renin

↓

formn of Angiotensin - II

↓

- Vasoconstriction
- Release of Aldosterone

(Major Long-Term regulator of BP)

↓

causes Na^+ & water reabsorption

↓

↑ses BP

→ ADH

Blood vol. ↓ses

↓

ADH secretes from Post. Pituitary

↓

↑ses water reabsorption from kidney

→ ANF (Atrial Natriuretic Peptide)

Blood vol. ↑ses

↓

Venous return ↑ses

↓

OPPO A53
2022/07

The synthesis of ANP in atria ↑

↓

causes Natriuresis & Diuresis

↓

↓ses BP

3. Neural Mechanism

1. Baroreceptor resetting & Central Adaptation

→ In chronic hypertension, Baroreceptors are reset to regulate the elevated BP.

→ Medullary cardiovascular centers also adapt to elevated pr.

2. Role of Sympathovagal Balance

Emotional response of the body & response to the environment are major stimuli for alternation in BP.

*HYPERTENSION (Applied)

→ Persistent High Blood Pr.

→ when systolic Pr. remains above 150 mm Hg & diastolic pr. remains elevated above 90 mm Hg, it is considered as Hypertension.

★ Types

1. 1° HT | Essential HP
2. 2° HT

OPPO A53
2022/07/15 23:25

1. **Primary HT** (also c/d Essential HT)
→ Elevated BP in the absence of any underlying disease
→ Arterial BP is ↑ed b/c of ↑ed peripheral resistance which occurs due to some unknown cause.
→ It is of 2 types :- Benign & Malignant
Benign → High BP that does not cause any problem & runs a relatively long and symptomless course.
Malignant → Severe form of HT with a rapid course leading to progressive cardiac & renal failure

2. 2° HT
→ Elevated BP due to some underlying disorder.
→ diffn forms of 2° HT are :-
1. Cardiovascular HT
2. Endocrine HT
3. Renal HT.
4. Neurogenic H.T.
5. HT during pregnancy

★ Experimental H.T.
→ HT produced in experimental animals by various methods
→ This HT is produced by :- Clamping Renal Ar., Injection of Corticosteroids, Infusion of salt with aldosterone.

Manifestations
1. Renal failure
2. Lt. Ventricular failure
3. Myocardial Infarction
4. Cerebral Hemorrhage

Treatment :- By using :-
1. Anti-adrenergic drug
2. Diuretics
3. Angiotensin converting Enzyme Inhibitors
4. Ca^{++} channel Blockers

OPPO A53

Date
Page

⑧ CORONARY CIRCULATION

→ Circulation of blood through blood vessels of heart muscles.

→ Responsible for functional blood supply to heart muscle itself.

→ It is about 4.7% of total cardiac output.

★ Coronary Blood Supply

1. Arterial Supply

→ Supplied by :- Rt & Lt coronary Artery
↓
originates from the root of the aorta behind ~~behind~~ Rt. & Lt. cusps of aortic valve.

Rt. coronary Ar. → supplies Rt. Ventricle & Rt. Atrium.
Lt. Coronary Ar. → " Lt. " & Lt. "

→ There is no anastomoses b/w Rt. & Lt. Coronary Ar. Thus the coronary arteries are end arteries in human being.

2. Venous Drainage

→ Has multiple venous drainage system.

Major System → consist of coronary sinus & Ant. Cardiac vein → drain into Rt Atrium

Minor system → consist of Arteriosinusoidal vessels, Thebsia vein.

OPPO A53
2022/07/

Date
Page

★ Special features

1. Heart receives its major blood supply during diastole.

↓ b/c

cardiac blood vessels are mechanically compressed during systole due to contraction of the ventricular muscles.

↓

∴ Blood flow during systole ↓ses to the Heart muscles

2. Coronary arteries are End arteries

↓

Blockage results in ischemia & Infarction

3. Metabolic regulation is well developed. Coronary blood flow is adjusted acc. to the need of the myocardium.

4. Unlike, cerebral circulation, significant alternation occurs in coronary circulation depending on cardiac activities.

5. Heart utilises wide variety of substrates for its metabolism major source of energy supply is free fatty acids.

6. Heart muscles extract about 80% of O_2 from arterial blood

★ Regulation of Coronary Blood flow

1. Neural Regulation

Sympathetic

↓

Stimulation produces ~~vasodilation~~ vasoconstriction

Parasympathetic → small innervation of coronary blood vessels

↓

Stimulation causes vasodilation

OPPO A53
2022/07/15 23:25

2. Metabolic Regulation

→ Metabolic Regulation of blood flow is well developed in Heart

→ Metabolic factors that causes coronary vasodilation are

↓

Hypoxia, ↑sed conc. of CO_2, ↑sed conc of H^+ & K^+

→ Adenosine → play an imp role in regulation of coronary blood flow

3. Autoregulation

→ Maintains a nrml blood flow within the pr. range of 70-110 mm Hg.

4. Physical factors

Blood flow to cardiac muscle is dependent on the myocardial tension, the pr. builds up in the muscle during contraction.

↓

1° factor in determining the coronary perfusion.

Applied

→ Angina Pectoris

- Angina literally means chest pain
- Angina pectoris refers to chest pain due to ischemia (inadequate blood supply) of the heart muscles.
- Common manifestation of **CAD**.
- Pain is felt in chest below the sternum towards the lt side

OPPO A53
2022/07/15 23:25

Date ______
Page ______

- Pain typically referred to ulnar border of the lt. hand, but can also radiate to back or even neck / abdomen.

Causes :- • Mainly due to hypoxia
• During myocardial ischemia there is accumulation of anaerobic metabolites end products (Uric acid), other pain producing sub. like sub P.

★ Chronic Angina Pectoris

→ Patient does not feel the pain nrmlly

→ Pain is felt only when the workload of heart ↑ses in conditions like exercise & emotional outburst.

→ when ν of angina attack ↑ses, patient is prone to develop acute myocardial infarction.

★ Tretment

1. By using drugs → Vasodilator drugs like Sodium nitrite relieve pain by dilating coronary arteries.

2. By thrombolysis

3. By surgical method → Aortic - Coronary Ar. bypass graft
↓

→ Part of myocardium affected by coronary occlusion is detected by anigography.

→ Then, anastomoses is made b/w aorta & Coronary Ar. beyond occlusion

→ Vein from lower limb is used for anastomoses.

OPPO A53
2022/07 15:23:25

⑨ **CUTANEOUS CIRCULATION**

→ **Triple Response**

- When skin is stroked firmly with a pointed ob., the response to injury is triple response.
- Has 3 main components :-

1. **Red Reaction**

→ Skin becomes red within 10 seconds.

→ Redness occurs due to capillary dilation that ↑ses capillary blood flow.

→ Dialation occurs due to direct response of capillary to pr.

2. **Wheal**

→ Swelling (local edema) is c/d wheal.

→ Occurs within few min following red rxn.

→ Occurs due to ↑sed permeability of capillaries

→ Histamine released from local mast cell causes vasodilation & ↑ses capillary permeability that results in leakage of fluid.

3. **Flare**

→ Spreading out of redness from site of injury to surrounding areas.

→ Occurs due to arteriolar dilation

$\downarrow$

occurs by activation of axon reflex

★ **Dermographism**

→ Process of embossing sign over skin, also k/n as writing skin.

→ Some letters can be embossed on skin in forearm in same manner by which wheal is produced.

OPPO A53
2022/07/15 23:25

Date
Page

⑩ SHOCK

→ general term that refers to the depression / suppression of body functions produced by any disorder.

★ Circulatory Shock

→ Shock developed by inadequate blood flow throughout the body

→ Life - threatening condn & it may result in death if person is not treated immediatly.

★ Characteristic features

→ Insufficient blood flow to tissues particularly the brain

↓

due to ↓sed C.O.

→ when C.O. ↓ses, arterial B.P. ↓ses

↓

causes reflex tachycardia & reflex vasoconstriction

↓

↓ses Stroke volume & systolic Pr.

↓

Hypoxia develops

↓

Skin becomes pale & cold, cyanosis develops in ear lobes & finger tips.

↓

Blood flow to vital organs is severely affected

↓

lack of blood flow to brain leads to ischemia

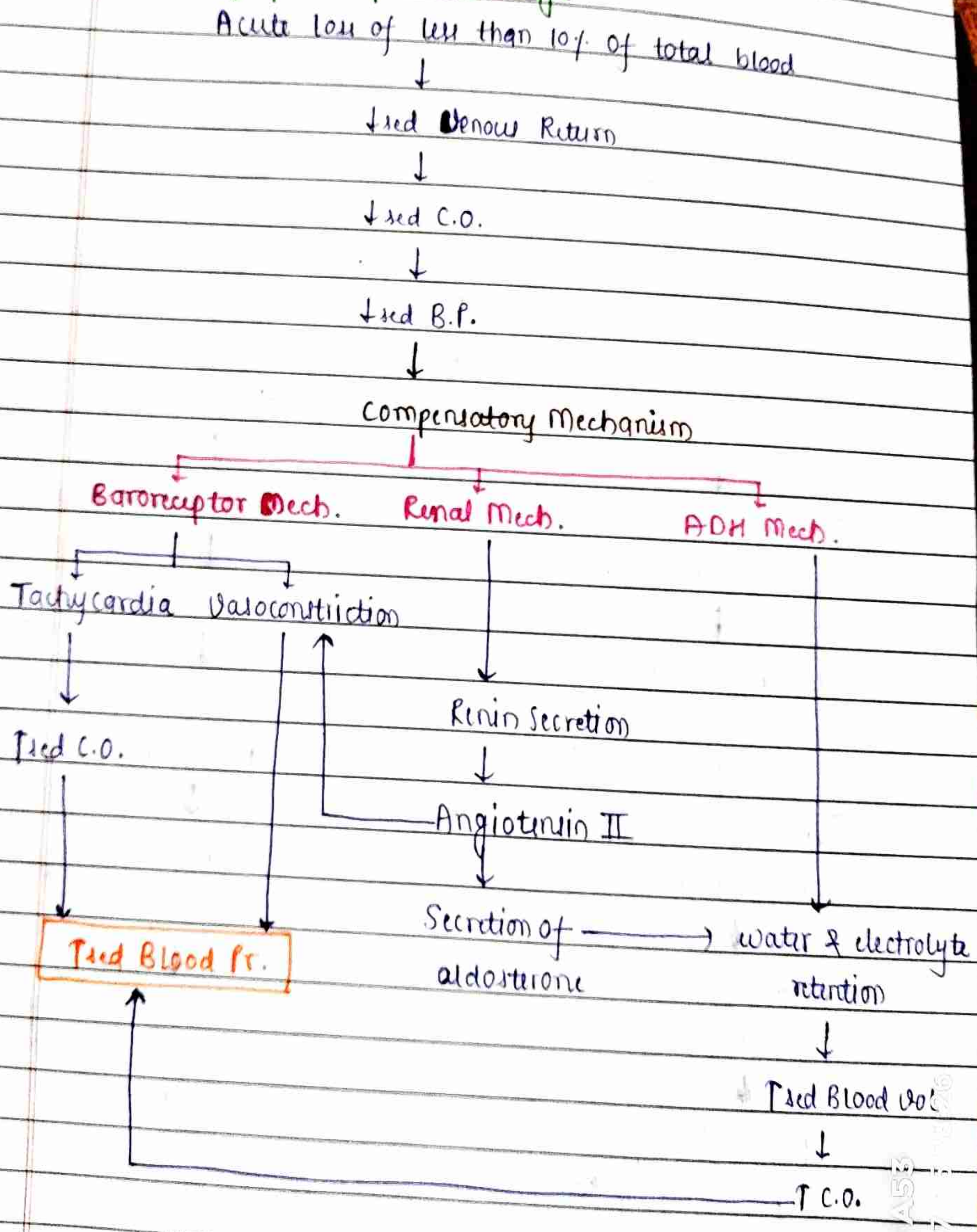
↓

damage of brain & cardiac arrest kill the victim

OPPO A53
2022/07 15 23:26

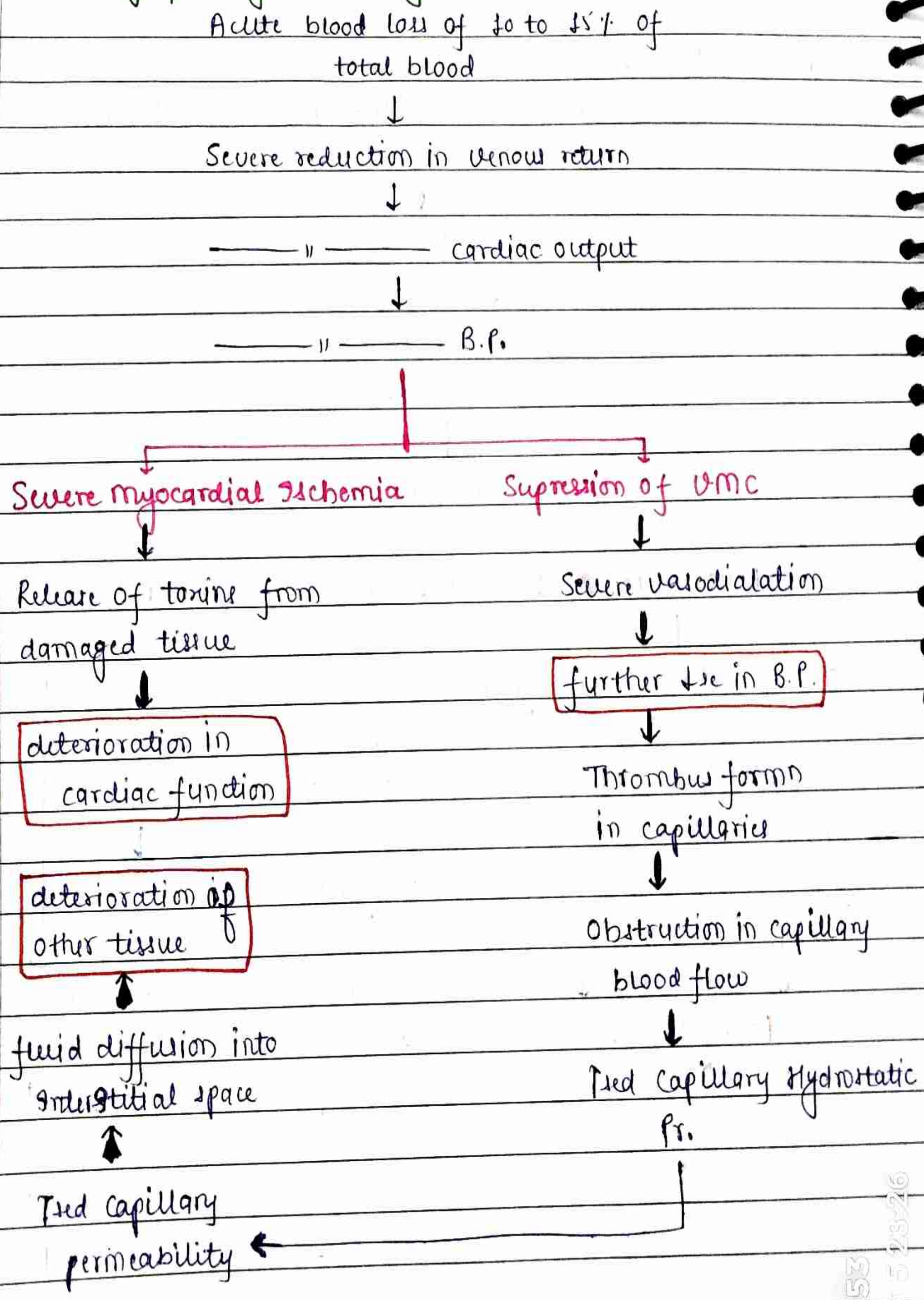
★ Stages of Circulatory Shock

1. 1st stage / Compensated stage


Acute loss of less than 10% of total blood
↓sed Venous Return
↓sed C.O.
↓sed B.P.
Compensatory Mechanism
Baroreceptor Mech.
Renal Mech.
ADH Mech.
Tachycardia
Vasoconstriction
↑sed C.O.
Renin Secretion
Angiotensin II
Secretion of aldosterone
water & electrolyte retention
↑sed Blood Vol
↑ C.O.
↑sed Blood Pr.

Date
Page

2. 2nd Stage / Progressive Stage



Acute blood loss of 30 to 35% of total blood

↓

Severe reduction in venous return

↓

—— " —— cardiac output

↓

—— " —— B.P.

Severe myocardial Ischemia

↓

Release of toxins from damaged tissue

↓

deterioration in cardiac function

deterioration of other tissue

↑

fluid diffusion into interstitial space

↑

↑sed capillary permeability

Supression of VMC

↓

Severe vasodialation

↓

further ↓se in B.P.

↓

Thrombus formn in capillaries

↓

Obstruction in capillary blood flow

↓

↑sed capillary Hydrostatic Pr.

3. **3rd Stage / Irreversible Stage**

→ Last stage also c/d Refractory Stage.

→ Irreversible → leads to death regardless of type of treatment offered to the patient.

↓

b/c brain fails to function due to severe cerebral ischemia

★ **Types of Circulatory Shock**

1. Shock due to ↓sed Blood Volume → Hypovolemic shock

Imp. Manifestations :-
1. ↓sed C.O.
2. ↓sed B.P.
3. Pale & Cold skin
4. ↑sed Respiratory Rate
5. Restlessness / lethargy

Occurs due to :-
1. Hemorrhage
2. Trauma
3. Surgery
4. Burns
5. Dehydration

★ **Hemorrhagic Shock**

→ Common hypovolemic & commonest of all shocks

→ Acute hemorrhage of more then 15 ml/kg body wt. result in shock.

OPPO A53
2022/07/15 23:26

Date ____
Page ____

Features :- 1. Hypotension
2. Tachycardia
3. Rapid pulse
4. Cold & Pale skin
5. Restlessness

Stages :- same as of Circulatory shock

★ Traumatic Shock
→ Occurs due to severe injury, especially when muscles & bones are extensively damaged.
→ Occurs in battlefield & road accident.

★ Surgical shock
→ Seen in surgical procedure with improper hemostasis
Rx^n to an injury that stops bleeding & repair damage
→ Occurs due to internal & external hemorrhage.

★ Burn shock
→ In burn, plasma is lost from burned surface as exudate
↓
(Plasma Protein + fluid)
→ Exudate does not contain RBC, so Hematocrit is high in burn shock.

2. Shock due to ↑sed Vascular Capacity → Distributive shock
Blood volume is nrml but B.P. ↓ses due to sudden ↑se in the capacity of the vascular compartment due to marked vasodilation.

OPPO A5s
2022/07/

Date
Page

→ May be of following types :- 1. Neurogenic shock
2. Anaphylactic shock
3. Septic shock

3. Shock due to Cardiac disease → Cardiogenic Shock

→ C.O. ↓ses due to ↓se ability of the heart to pump blood.

→ Seen in :-

1. Acute Myocardial Infarction
2. Heart failure
3. Cardiac arrhythmias

4. Shock due to obstruction of blood flow → Obstructive Shock

→ C.O. ↓sed b/c of obstruction to the ejection of blood from the ventricles.

→ Seen in :-

1. Cardiac Tamponade
2. Constrictive pericarditis
3. Cardiac tumor

OPPO A53
2022/07/1

Date 25/11/21
Page

RESPIRATORY SYSTEM **

① PULMONARY CIRCULATION

→ Amount of Blood ejected into pulmonary circulation
↓
same as the amount ejected into Systemic circulation

→ Pulmonary (P.C.) circulation = low pr. circulation
Systemic (S.C.) —"— = High —"—

→ Total resistant in P.C. = $\frac{1}{10}$ th of S.C.

★ **functions**

1. Gas Exchange → Bring venous blood from diffⁿ parts of body for exchange of gases in alveoli.

2. Serves as a filter → filters thrombi (blood clots) & emboli

3. metabolic function → Angiotensin I $\xrightarrow{\boxed{ACE}}$ Angiotensin II
↓
Pnt in pulmonary capillary endothelial cell.

→ Pulmonary capillary Endothelial cells $\xrightarrow[\text{inactivates}]{}$ Bradykinin, Serotonin & Prostaglandins.

4. Serves as a blood reservoir → About 500ml of blood is Pnt in P.C. at any point of time

OPPO A53
2022/07/15 23:26

* Characteristic features of Pulmonary Circulation

1. P.C. is low Pr. & low resistance system.

2. Pulmonary Ar. have thin walls, that's why they are more compliant
↓
Due to high compliance can accomodate a relatively large amount of blood whenever required.

3. Pulmonary arterioles are also thin walled
↓
∴ ability to constrict is less

4. Pulmonary veins → thin walled & highly compliant.

5. Pulmonary capillaries do not form a capillary network instead they form lattice in alveolar wall so that blood flows as a thin sheet.

6. Change in pulmonary venous & lt. atrial pressure affects the gas exchange. → measured by wedge pressure.

7. Pulmonary vascular (PVR) resistance is very low, about 1/10th of systemic vascular resistance due to
   i) High compliance of P. arterioles.
   ii) Resting vasoconstrictor tone is very low (arterioles are mostly dilated)

8. Unique feature → PVR falls with ↑sed Pulmonary Arterial Pr.

OPPO A53
2022/07/5 23:26

due to 2 mechanisms :-

i) Capillary Recruitment → when blood flow ↑ses (C.O. ↑ses)
↓
collapsed vessels are opened
↓
↓ses the overall PVR instead of ↑sed C.O.

ii) Capillary Distension → Occurs b/c P. capillaries are thin & highly compliant.

★ Significance of Low Pulmonary Vascular Resistance (PVR)
→ Has 3 beneficial effects

1. ↓sed resistance, ↓ses the velocity
↓
provides adequate time for P. Capillaries blood to take O_2 & dispose CO_2.

2. Capillary distension ↓ses the resistance & ↑ses capillary surface area
↓
facilitates diffusion of gases

3. ↓se in PVR, ↓ses the load on R. ventricles & lowers the capillary Pr. that Prevents pulmonary edema.

OPPO A53

② RESPIRATORY MEMBRANE

→ also c/d Alveolar capillary membrane.
→ forms blood-gas interface that separates blood in P. capillaries from gas in alveoli.

- Diffusion of gases takes place through this membrane.
- mem. is exceedingly thin & composed of alveolar epi., interstitial fluid & capillary Endothelium.
- O_2 & CO_2 moves across the blood-air interface by diffusion

★ Layers of Membrane

→ Alveolar capillary interface consist of 6 layers
→ But, O_2 from P. capillaries enter alveolar lumen by passing through 10 layers

1. Alveolar Surfactant
2. Layers of Alveolar Epithelium
3. Basement mem. of — " —
4. Thin layer of interstitial fluid
5. Basement mem. of Capillary Endothelium
6. Layers of Capillary Endothelial cells
7. Plasma
8. Red cell mem.
9. Intra-erythrocyte fluid
10. Hb-molecule

Thickness → 0.2-0.5 μ (allow easy diffusion of gases)

★ Factors Affecting Diffusion of gases

1. Difference in Partial Pr. of gas on both side of mem.

OPPO A53
2022/07/ 5 23:

Date ______
Page ______

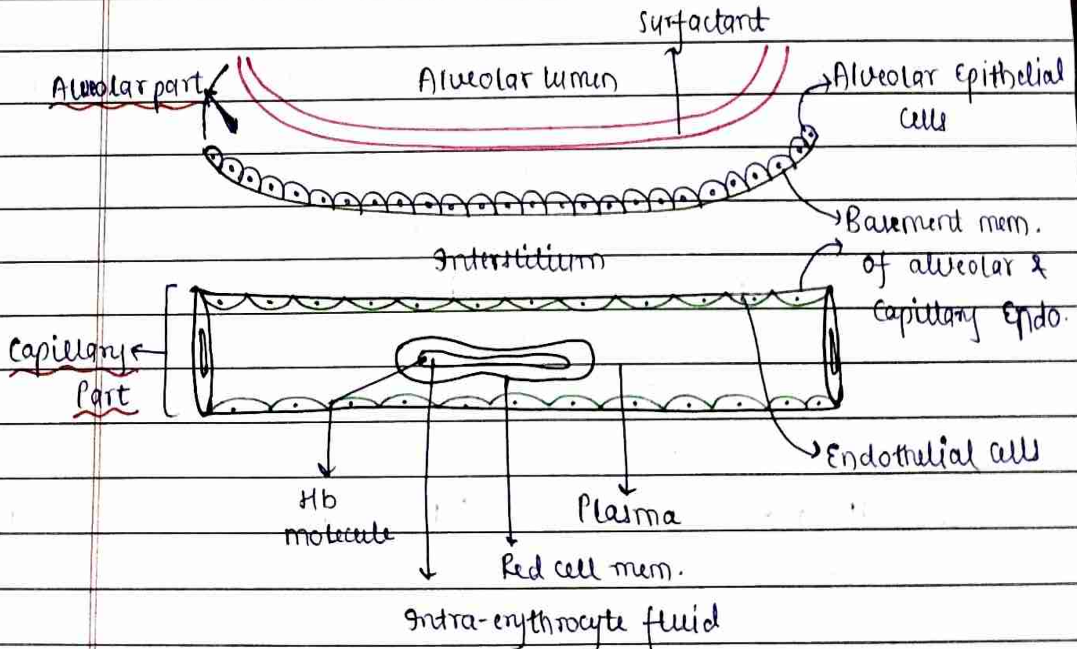
2. Diffusing capacity of mem. for gases

3. Surface area of mem. → ↓ses in Emphysema
↑ses in Exercise

4. Solubility of gases → CO_2 more soluble then O_2

5. Thickness of mem. → Diffusion ∝ $\frac{1}{\text{thickness}}$

6. Molecular wt. of gas → Diffusion ∝ $\frac{1}{\text{Mol. wt.}}$


Surfactant
Alveolar part
Alveolar lumen
Alveolar epithelial cells
Basement mem. of alveolar & capillary Endo.
Interstitium
Capillary Part
Endothelial cells
Hb molecule
Plasma
Red cell mem.
Intra-erythrocyte fluid

★ Layers of Respiratory Mem.

OPPO A53
2022/07

Date ______
Page ______

★ Clinical

Alveolar Capillary Obstruction Syndrome

→ Occurs in 2 imp. types of defects

1. Thickening of Alveolar - Capillary membrane
→ seen in interstitial fibrosis.

2. Increased distance b/w Alveolar & Capillary membrane due to interstitial edema (seen in heart failure)

★ In this syndrome, diffusion of gases is ↓ed (mainly O_2 but not CO_2) b/c :-

↓

Both O_2 & CO_2 are soluble in lipid but CO_2 is 20 times more soluble in water then O_2.

↓

so, in interstitial edema fluid accumulates b/w the alveolar & capillary mem.

↓

diffusion of CO_2 is not hampered.

∴ Hypoxemia develops without significant change in P_{CO_2}.

★ CO Method

→ CO transport is diffusion limited

↓

- readily diffuses across mem. but due to high affinity for Hb, rapidly binds to Hb.
- This ↓ses Partial Pr. of CO in blood, so eqm of CO is never reached across the mem.

OPPO A53

③ Mechanism of Breathing

→ It is the study of physical properties of lung, airways and chest wall involved in the physiology of respiration.

★ **Muscles of Respiration**

1. Muscles of Inspiration

→ Causes expansion of chest and ↑es the elastic recoil of chest wall.

→ This makes intrapleural pr. more (-)ve.

- 1° muscles of Inspiration

Diaphragm & the ext. intercostal muscles

Diaphragm → • main muscle of inspiration, inflation of lung is caused 1°ly by contraction of diaphragm.

• Diaphragm is innervated by phrenic N. $(C_3-C_5$ cervical root) & lesions of these nerves leads to paralysis of that side of diaphram

↓

so, diaphragm of that side moves up rather then coming down during inspiration

Ext. Intercostal Muscles → • Present obliquely b/w ribs in forward & downwards direⁿ.

• Contraction of these muscles has 2 effects :-

1. Tr. & AP diameter of thorax ↑es → by 2 mechanisms.

Bucket Handle effect → ↑es Tr. diameter

Pump Handle effect → ↑es vertical diameter

OPPO A53

2. Rib cage & tissue b/w the ribs becomes stiff

- Accessory muscles of Inspiration

→ assist in forced inspiration
· Scalenus (muscle of neck)
Sternocleidomastoids
Neck & Back muscles
muscles of upper respiratory tract

2. Muscles of Expiration

→ When inspiration ends, inspiratory muscles relax, rib cage drops & thoracic vol. ↓ses. The elastic recoil of lung is now unopposed, this results in expiration

→ Quiet Exp. → passive process, so no 1° muscle of exp. are there

→ During forced exp., accessory muscles are involved that includes abdominal muscles, inter intercostals & neck & ~~rib~~ back muscle

Abdominal muscles → · Includes int. oblique, ext. oblique, transverse abdominus
· Contraction ↑ses Intra-abdominal pr. & push diaphragm upwards.

Intercostal (Internal) → · pull the rib cage downwards & ↓ses the thoracic volume, both in Antero-posterior (AP) & Tr. diameter (helpful in coughing, vomiting)

Neck & Back muscles → ↓ses the cross-sectional area of thorax.

OPPO A53
2022/07/15 23:27

★ Pressure change during Breathing

1. Intrapleural Pr.
2. Transmural Pr.
3. Alveolar Pr.

1. Intrapleural Pr. → • Pr. in the pleural space i.e., in b/w the Parietal & Visceral layer of pleura.

★ Cause for Negativity of Pr.

- lung recoils inwardly and chest wall recoils outwardly, these equal and opposing forces causes the pr. to be (-)ve.
- It is (-)ve during quite breathing & more (-)ve during ~~forced~~ deep inspiration.
- In forced expiration, it may become (+) ve.

★ Normal values

During Expiration → -2.5 to -4 mg Hg
During Inspiration → -6 mg Hg
→ Quite Breathing

During Expiration → positive
During Inspiration → -30 mm Hg
→ forced Breathing

★ Measurement

1. By inserting a needle into intrapleural space, not safe to introduce b/c it may result in pneumothorax.
2. By recording intraesophageal pr. by introducing a balloon catheter through mouth into esophagus.

★ Significance

Physiolog-ical 1. Facilitates Inspiration & maintains shape of chest + size of lungs.

Clinical 2. Pneumothorax (accumulation of air in pleural space)

OPPO A53
2022/07/ 5 23:

Date ______
Page ______

2. **Transmural Pressure** → • Pr. diff. across the airway or across the lung wall.

• 2 major transmural Pr. are :-

Transpulmonary Pr. → • Pr. diff across the lung wall
- keeps lungs inflated & prevents them from collapsing.
- always (+)ve during nrml breathing

Transairway Pr. → • Pr. diff across the airway
- Imp. in keeping airway open during forced expiration.

3. **Alveolar Pressure** → • Pr. inside the alveoli

• change in this pr. moves the air in and out of lung.

• During Inspiration → ↓ses that sucks the air into the lung.

During Exp. → ↑ses that moves air out from the lung.

★ Nrml value → -1 mm Hg (Inspiration)
+1 mm Hg (during Exp.)

★ Types of Breathing

1. **Abdomino-Thoracic** → • seen in males
2. **Thoraco-Abdominal** → • seen in females & children

OPPO A53
2022/07 15 23:27

Date
Page

★ Sequence of Events during Inspiration

Contraction of diaphragm & other inspiratory muscles
↓
Expansion of thoracic cage
↓
Intrapleural Pr. becomes more (-) ve
↓
↑se in ~~Intra-alveot~~ Trans-pulmonary Pr.
↓
Inflation of lung
↓
↓se in alveolar Pr. (becomes subatmospheric)
↓
Air flows into airways & lungs
↓
End of contraction of muscles & end of inspiration.

★ Sequence of Events during Expiration

Relaxation of Inspiratory muscles
↓
Dropping of rib cage
↓
Intrapleural pr. becomes less (-) ve
↓
↓se in trans-pulmonary pr.
↓
Deflation (recoil) of stretched lung
↓
↓se in alveolar diameter
↓

OPPO A53

Rse in Alveolar Pr. (greater then atmospheric pr.)

↓

Air is pushed out of lung

↓

Expiration continues until alveolar pr.
equals atm pr.

OPPO A53

④ PULOMNARY SURFACTANT

- → Surface acting material responsible for lowering surface Tension of fluid
- → mixture of lipoprotein rich in phospholipids.
- → Principle surface tension lowering agent in surfactant is ~~dimethylphosphatidylcholine (DMP~~ dipalmitoylphosphatidylcholine (DPPC) / dipalmitoyl-lecthin (DP

- → Alveolar surface Tension $\propto \dfrac{1}{\text{conc. of Phospholipids in surfactant}}$

★ Source

- → Synthesised in Type II - Pneumocytes
- → There are 2 types of cells in alveolar epithelium.
- → Alveolar type II cells are c/d Type-II Pneumocytes.

↓

Ratio b/w type I & type II = 1:1

- → Type-I cells form about 2/3rd of surface area
- → Type-II are metabolically more active & contain more no. of mitochondria.

↓

Special feature → presence of electron-dense lamellar inclusion bodies. (~~stores~~ stores surfactant in type II cells)

★ Synthesis & Secretion

- → Palmitate, choline & glucose → substrate molecule

- → Released lamellar body - materials are converted into tubular myelin that forms the film of surfactant on the alveolar surface.

OPPO A53
2022/07/1 5 23:27

★ Steps of Secretion

Substrate molecules (palmitate, choline, glucose) are picked up from blood by Tye-II pneumocyte

↓

Substrate molecules are synthesised into DPPC in mitochondria

Protein component is formed in endoplasmic reticulum

↓ ↓

DPPC & proteins are packaged in Golgi apparatus

↓

Materials are stored in lamellar bodies (LBs)

↓

LBs from type-II pneumocyte are discharged towards the surface of alveolar epithelium by exocytosis

↓

LB material converted to tubular myelin (TM)

↓

TM forms phospholipid film on alveolar epithelium surface

★ Regulation of Synthesis & Secretion

1. Hormonal factors

- Glucocorticoids → Cortisol stimulates surfactant synthesis.
- Thyroxine → promotes synthesis
- Insulin → promotes synthesis

2. Quantity & Quality of Proteins in Surfactant

- formn is greatly facilitated by protein ⊕nt in surfactant

↓

Proteins are albumin, immunoglobulin-A & Apo-proteins

OPPO A53
2022/07/15 23:27

Date
Page

3. Stretching of lungs
Hyperinflation of lungs like yawning enhance synthesis.

★ **Functions**

1. Prevents lung collapse
By ↓sing surface Tension at air-liquid interface of alveoli, surfactant prevents lungs collapse.

2. Promotes alveolar stability
By preventing the collapse of smaller alveoli.

3. Helps to prevent edema
Inward force of Surface Tension ⟶ collapse alveoli
↓
pulls fluid out of capillaries ⟵ ↓sed Interstitial Pr.
↓
& leads to pulmonary edema formn.

Surfactant reduces surface force & thus prevents pulmonary edema formn.

4. On work of Breathing
↓ses ——— " ———. so breathing becomes easier.

5. On Immunity
IgA & apoproteins provides innate immunity by acting as opsonins.

OPPO A53
2022/07/15 18:27

★ Clinical

1. Infant Respiratory Distress Syndrome | Hyaline Membrane disease

→ Surfactant helps in lung inflation & prevents collapse.

→ In case of premature infants, due to lack of surfactant synthesis lung expansion becomes difficult
↓
breathing becomes extremely labored due to high S.T. & becomes difficult to inflate lung.

- Treatment

1. Administration of phospholipids by inhalation
2. Inhalation of synthetic surfactant
3. Glucocorticoid theraphy

OPPO A53
2022/07/15 23:28

⑤ LUNG COMPLIANCE

- → Ability to stretch / ability to recoil.
- → lung compliance can be assessed by pressure - volume curve.
- → Compliance is the measure of distensibility of lung.
- → Represented by, change in volume per unit change in pressure.

$$C = \frac{\Delta V}{\Delta P}$$

★ Measurement of lung compliance

1. Static lung compliance Measurement

→ Measured by analysing the Pr. - vol relationship.

★ **Pr. - Vol Relationship** → obtained for human lungs by simultaneously measuring change in lung vol. & change in pleural pr.

- → For recording, the individual expires maximally to TLC & then expires slowly.
- → The compliance recorded in these condn, is c/d Static lung compliance, as airflow does not occur.
- → As lung is deflated from TLC, deflation pr- vol curve is obtained.
- → To obtain, inflation pr- vol. curve lung is inflated from FRC to TLC.

→ Stages of Pr - Vol Curve

1. Stage of Stable Lung vol.

↓

2. Stage of opening of airways

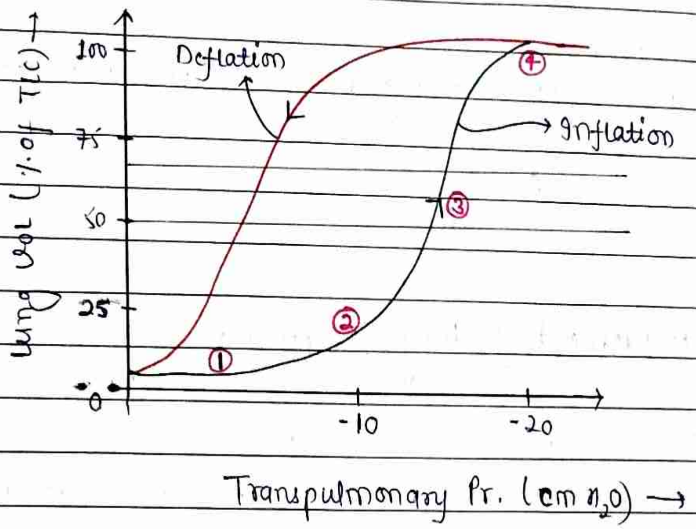
↓

OPPO A53

3. Stage of linear ↑se in lung volume

↓

4. Stage of cessation of Inflation



Diff b/w inflation & deflation pr.-vol curve, k/n as **Hysteresis loop**.

2. Dynamic lung Compliance Measurement

→ Mechanism in play when the lungs are in motion.

→ Obtained by continuously measuring the change in intrapleural pr. & lung vol.

→ Pattern of curve obtained is similar to that of static the only diff is that dynamic compliance is less than its static compliance.

★ Factors affecting

1 Distensibility & Elastic Recoil → directly ∝
2. lung volume → inversely ∝
3. lung size → directly ∝
4. Surface Tension inside Alveoli

OPPO A53
2022/07/15 23:28

★ Clinical Significance

1. Low Compliance

→ Indicates less distensibility means more work is required to inflate the lung.

→ ↓ses in cond^n such as :-

1. Pulmonary fibrosis
2. Paralysis of respiratory muscles
3. Pleural effusion
4. Abnrml thorax, such as pneumo-thorax, hydrothorax.

2. High Compliance

→ Occurs due to loss of elastic property of lung tissue

→ occurs in cond^n such as :-

Physiological → Old age
Pathological → Emphysema
↓

- Occurs in chronic habitual smokers
- Lung tissue is destroyed by elastase released from microphages.
- In this disease, easy to inflate lung & the elastic recoil of lung is much less.
- Have abnormlly High RV

OPPO A53
2022/07/15 21:28

⑥ WORK OF BREATHING

→ During breathing, work is done to expand the lung & overcome the airway resistance.

→ During inspiration work is done to :-
  1. Expand the thoracic cavity
  2. Inflate the lung
  3. Overcome airway resistance

→ Work = change in lung vol. x change in trans-pulmonary Pr.

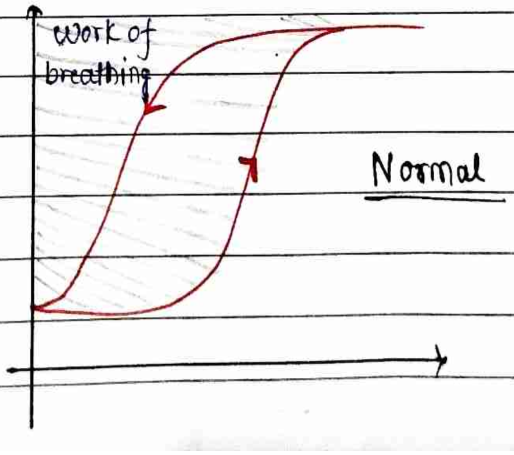
$$\boxed{W = P \times \Delta V}$$

→ Energy is spent with muscular contraction to create a force (Transpulmonary Pr.) to ↑se the lung vol. (inflate the lungs)

→ More muscular work ⟶ more transpulmonary Pr.
↓
bring more air into lung

→ The P-V curve depicts the work required in nrml breathing
↓
that spends 5% of body's total energy expenditure

→ During Exercise, Energy Expenditure is ↑ed.



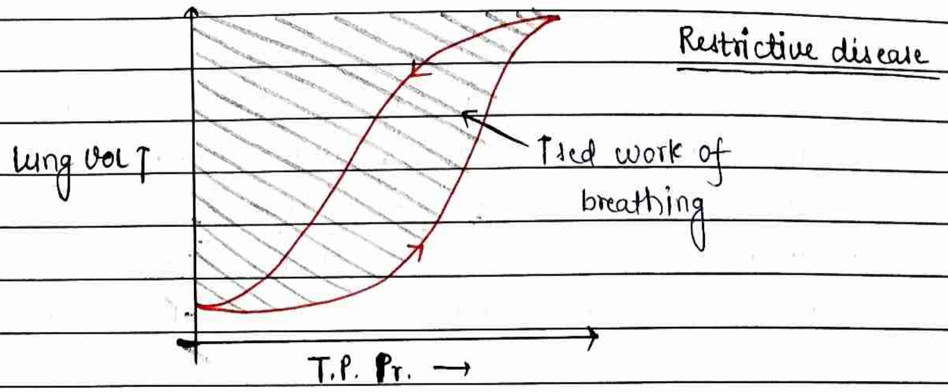
OPPO A53
2022/07 5 23:28

★ Applied

1. Restrictive lung Disease

→ work of Breathing is ↑ed, as greater inspiratory effort is required due to ↓se in lung compliance.

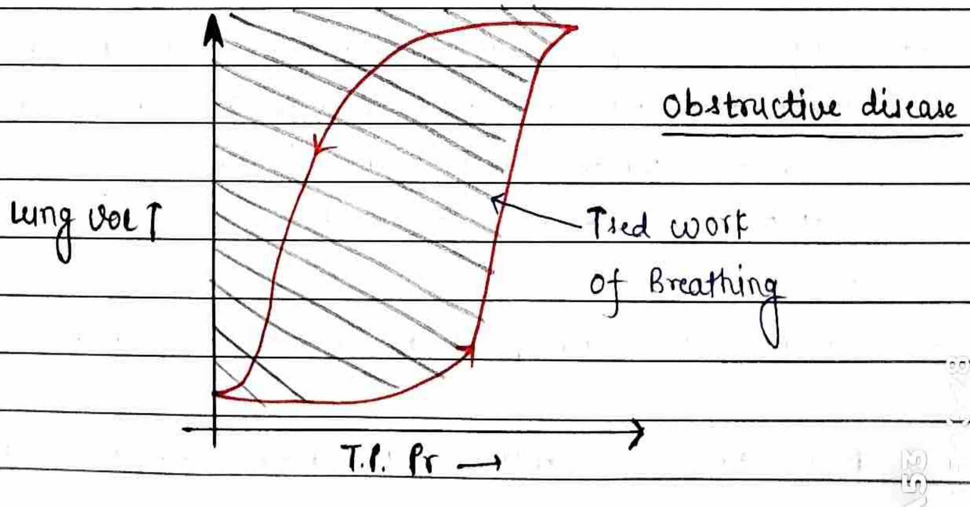
Patients take rapid & shallow breath.


Restrictive disease
lung vol ↑
T.P. Pr. →
↑ed work of breathing

*2. Obstructive lung Disease

→ Work of Breathing ↑se due to more expenditure of energy to overcome ↑ed airway resistance

Patients take slow & deep breath.


Obstructive disease
lung vol ↑
T.P. Pr →
↑ed work of Breathing

Date ______
Page ______

⑦ PULMONARY VENTILATION

→ Ventilation is the rate at which air enters or leaves the lung.

★ **Types**

1. Pulmonary Ventilation

→ Volume of air moving in and out of respiratory tract in a given unit of time, during quiet breathing.

→ also c/d Minute Ventilation / Respiratory minute Volume (RMV)

→ It is a cyclic process by which, fresh air moves in lung and an equal vol. of air leaves the lung.

Nrml value :- $\boxed{P.V. = TV \times \text{Respiratory Rate}}$ $= 500 \times 12$

$= 6{,}000$ ml

$= 6$ L/min

↓

In adult → 5-10 L/min

2. Alveolar Ventilation

→ Amount of air utilised for gaseous exchange every min.

→ Diffⁿ from pulmonary ventilation, as in Pulmonary ventilation 6 L of air moves in & out of tract every min. but whole vol. is not utilised for exchange vol of air subjected for exchange of gases is alveolar ventilation.

→ Air trapped (dead space) does not take part in exchange.

Nrml value :- $A.V. = (TV - \text{Dead Space}) \times \text{Resp. Rate}$

$= (500 - 150) \times 12$

$= 4{,}200$ ml

$= 4.2$ L/min

OPPO A53
2022/07/15 23:28

Date ______
Page ______

Dead Space

→ Part of respiratory tract, where gaseous exchange does not take place.

→ Air ⊕nt is k/n as Dead Space Air.

→ The fraction of TV that occupies the conducting airway does not take part in gas exchange.

↓

For each 500 ml inhaled, about 150 ml remains in conducting airway & not used in exchange

↓

This wasted air is k/n as Dead Space Volume

★ Physiological Dead Space

→ Physiological Dead Space = anatomical D.S. X Alveolar D.S.

- Dead space is due to structural arrangement of airways, so c/d Anatomical D.S.
- Some alveoli due to some reasons have little or no blood supply, the vol. of air in these alveoli is wasted air & is c/d Alveolar D.S.

→ Nrmlly, Alveolar D.S. is negligible so anatomical D.S. is almost equal with physiological dead space.

→ In lung disease, alveolar D.S. is high, so physiological D.S. > Anatomical D.S.

★ Measurement of Dead Space

1. Radford's Method
2. Single-Breath CO_2 Technique
3. ——||—— Nitrogen Technique

OPPO A53
2022/07/15 23:28

⑧ LUNG VOLUME & CAPACITIES

★ Lung Volumes

1. Tidal Volume (TV) → 500 ml
Volume of air inspired or expired during quite breathing

2. Inspiratory Reserve Volume (IRV) → 3,300 ml
Additional vol. of air that can be inspired forcefully after the end of nrml inspiration

3. Expiratory Reserve Volume → 1000 ml
Additional vol. of air that can be expired out forcefully after nrml expiation

4. Residual Volume → 1200 ml
Vol. of air remaining in lungs even after forced expiration
Significant b/c of 2 reasons :-
1) Help to aerate the blood in b/w breathing & during expiration
2) Maintains the contour of lungs

★ Lung Capacities

1. Inspiratory Capacity → 3800 ml
Maxm vol. of air that is inspired after nrml expiration

$\boxed{IC = TV + IRV}$

OPPO A53
2022/07/ 15:23:28

2. Vital Capacity → 4800 ml

Max^{m} vol. of air that can be expelled out forcefully after a deep (max^{m}) inspiration

$$\boxed{VC = TV + IRV + ERV}$$

★ Variation of Vital Capacity

1. Physiological Variation

Sex :- In females VC is less then males

Body Built :- More in heavily built person

Posture :- More in standing & less in lying

Athletes :- More in athletes

Occupation :- Incd in people who play wind instruments (flute)

2. Pathological Variation

↓ses in following cond^{n} :- 1 Asthma
2. Emphysema
3. Pneumonia
4. Pulmonary T.B.
5. Pneumothorax
6. Hydrothorax
7. Hemothorax

★ Measurement

By Spirometry (sub takes deep inspiration & expires forcefully)

3. Functional Residual Capacity → 2200 ml

Vol of air remaining in lungs after nrml expiration.

$$\boxed{FRC = RV + ERV}$$

OPPO A53
2022/07/15 23:28

7. Total lung capacity → 6000 ml

Vol. of air ⊕nt in lungs after deep (maximal) inspiration

$\boxed{TLC = IRV + TV + ERV + RV}$

facts

→ **Residual Vol.** = cannot be measured by spirometry.

→ capacities which includes RV also cannot be measured (FRC & TLC)

↓

They all are measured by Nitrogen washout technique/ Helium dilution technique/ Body Plethysmograph

OPPO A53
2022/07 15 23:28

Date
Page

⑨ **OXYGEN TRANSPORT**

→ Tranported from alveoli to tissue by blood in 2 forms:-
As simple physical soln
In combination with Hb

1. In Physically dissolved form
→ O_2 dissolves in water of plasma & transported in physical form.
→ It forms about 3% of total O_2 in blood.
→ Transport in this form becomes imp. during exercise to meet the excess demand of O_2.

2. In combination with Hb
→ O_2 + Hb = Oxy-Hb

→ It is about 97% of total O_2 in blood & is imp. b/c maxm amount is transported in this form.

* Oxygenation of Hb
→ O_2 combines with Hb only as a physical combination
↓
It is oxygenation & not oxidn b/c after combination Fe remains in Fe^{+2} (ferrous) form only

→ O_2 combines with Iron in Heme part of Hb.
→ Each molecule of Hb $\xrightarrow{\text{contains}}$ 4-atoms of Fe
→ Each Fe atom $\xrightarrow[\text{with}]{\text{combines}}$ 1-molecule of O_2

OPPO A53
2022/07/15 23:28

★ O_2 Carrying Capacity of Hb

Amount of O_2 transported by 1 gm of Hb.

$$\star\ 1\text{ gm Hb} \xrightarrow{\text{binds}} 1.34\text{ ml of } O_2$$

★ O_2 carrying capacity of Blood

→ Amount of O_2 transported by blood.

→ Nrml Hb content in blood is 15 gm%. & 1 gm Hb carries 1.34 ml O_2.

$$\therefore\ 1.34 \times 15 = 20.1\text{ ml } O_2 / 100\text{ ml of Blood}$$

O_2 carrying capacity of arterial blood is 20 ml O_2 per 100 ml of blood.

★ Saturation of Hb with O_2

→ Saturation is the state when Hb is unable to carry any more O_2.

→ Saturation of Hb with O_2 depends on :- Partial Pr. of O_2

↓

explained by O_2 - Hb dissociation Curve

O_2 - Hb Dissociation Curve

→ Explains Hb - affinity for O_2.

→ Demonstrates the relationship b/w PO_2 & percentage saturation of Hb with O_2.

→ Curve is S-shaped over the range of PO_2 from 0 mmHg to 100 mg Hb.

→ As PO_2 rises, Hb saturation also ↑ses.

→ Saturation is not linear with ↑se in PO_2

OPPO A53
2022/07/ 5 18:28

Date
Page

→ Curve is divided into 2 major phases :-

1. Steep Phase
2. Plateau Phase

★ Steep Phase

→ Curve has steep slope b/w PO_2 of 10 mm Hg & 60 mm Hg.

→ During this phase, combination of O_2 with Hb ↑ses very rapidly as PO_2 ↑ses from 10 to 60 mm Hg.

→ O_2 - saturation of Hb is about 90% at PO_2 60 mm Hg.

★ Plateau Phase

→ Curve begins to plateau at PO_2 around 60 mm Hg & flattens at PO_2 of 70 mm Hg.

→ ↑se in PO_2 above 60 mm Hg produces only a small ↑se in O_2 - binding.

→ ↑se in PO_2 from 60 to 100 mm Hg illustrates that O_2 - saturation & content remains apparently constant over a wide alteration in alveolar PO_2.

★ The P_{50}

→ P_{50} is the partial pr. of O_2 at which Hb saturation with O_2 is 50%.

→ P_{50} asses the binding affinity of Hb for O_2.

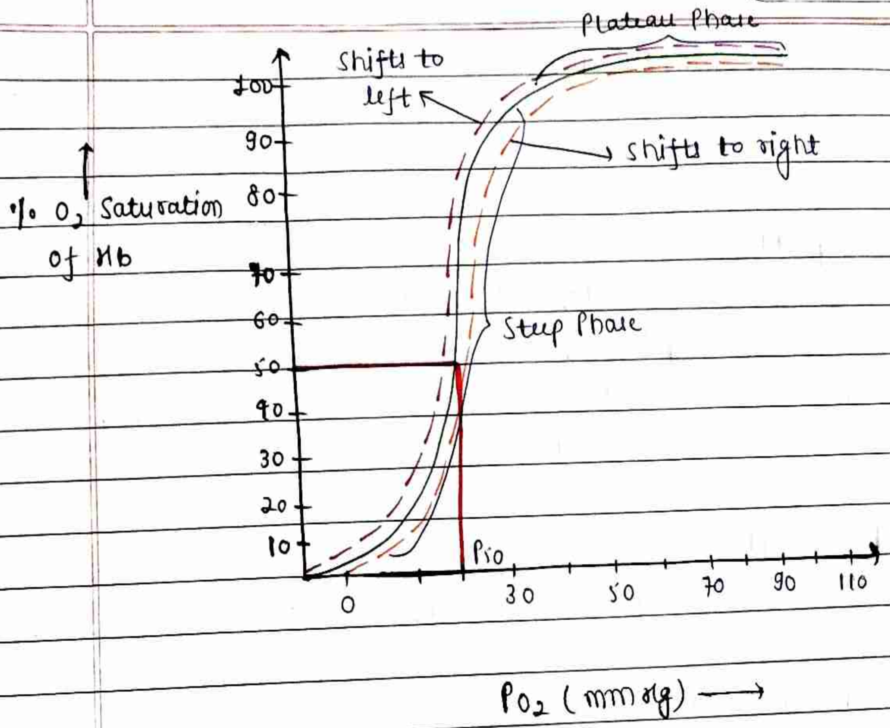
→ In adult, P_{50} occurs at PO_2 of 27 mm Hg

→ Alteration in P_{50} has great impact on steep phase of curve.

→ If P_{50} is high → signifies ↓se in affinity of Hb for O_2.

→ If P_{50} is low → signifies ↑se in affinity of Hb for O_2.

OPPO A53



★ Factors affecting O_2-Hb dissociation curve

1. Shifts to Right

→ Shifts in following condn

- ↓se in Po_2
- ↑se in Pco_2
- ↑se in H^+ ion conc
- ↑se in body temp.
- ↑se in 2,3 DPG (Biphosphoglycerate) conc.

↓

Byproduct in Embden - Mayerhoff pathway of carbohydrate metabolism in RBC.

2. Shifts to left

OPPO A53
2022/07/15 23:28

Date ____
Page ____

- ↓se Temp
- ↑ pH
- ↓ PO_2
- ↓ 2,3 DPG
- Fetal Hb
- CO

★ O_2 delivery to Tissue

→ Occurs along conc. gradient of O_2 from High level to low level.

→ PO_2 in systemic capillary blood is 95 mm Hg, whereas PO_2 in interstitial fluid is 40 mm Hg.

↓

This large pr. diffⁿ of O_2 causes O_2 to diffuse rapidly from capillary blood into interstitial fluid.

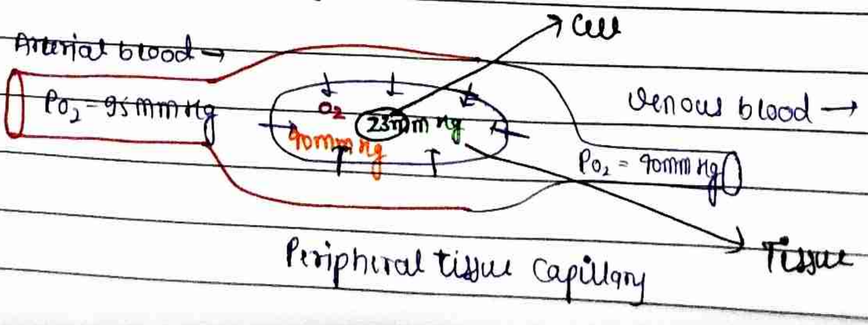
→ From tissue fluid, O_2 enters the cell as in the intra-cellular fluid the PO_2 is about 23 mm Hg.

★ Diffusion of O_2 to tissue depends on 2 imp factors :-

i) Rate of flow of blood to tissue

ii) Rate of tissue metabolism

∴ O_2 delivery is more if blood flow is more & metabolic activity is more.


Cell
Arterial blood →
PO_2 - 95 mm Hg
O_2
23 mm Hg
40 mm Hg
Venous blood →
PO_2 = 40 mm Hg
Tissue
Peripheral tissue capillary

OPPO A53
2022/07

★★ Bohr Effect

→ Any factor that shifts O_2 - Hb dissociation curve to right ↓se affinity of O_2 for Hb.

→ At tissue level, CO_2 enters the blood & shifts the curve to right. This helps in unloading of O_2 from Hb & facilitates tissue oxygenation.

↓

This is Bohr Effect

→ At tissue, due to continuous metabolic activities, P_{CO_2} is very high & P_{O_2} is very low.

★ It helps in unloading of O_2 & loading of CO_2

→ Factors influencing the Bohr Effect
All factors, which shifts the curve to rights

OPPO A53
2022/07 5 23:29

Date ______
Page ______

⑩ CARBON DIOXIDE TRANSPORT

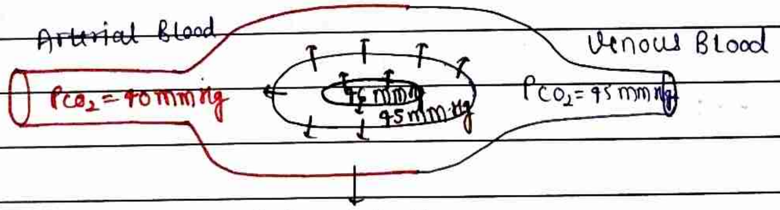
→ CO_2 is transported by the blood from cells to the alveoli.
→ CO_2 is transported in blood 3 forms :-
1. Physically dissolve in Plasma (7%)
2. As bicarbonate ion in plasma & in red cells (70%)
3. As carbamino-protein complex (23%)

1. As dissolved form

→ CO_2 diffuses into blood & dissolve in the plasma & is transported as dissolved state.

→ The solubility cofficient of CO_2 is 20 time greater than that of O_2 i.e., 0.06 ml/dl/mm Hg.

→ Due to absence of carbonic anhydrase in plasma, carbonic acid formn is negligible in plasma.



Peripheral tissue
capillary

2. As Bicarbonate

→ About 70% CO_2 travels in this form, this become possible due to presence of large quantity of carbonic anhydrase in red cells.

→ From tissue, CO_2 is released in plasma
↓
CO_2 diffuses into Red cells

OPPO A53
2022/07 15 23:29

In red cells, it forms either H_2CO_3 or Carbamino-Hb

↓

$CO_2 + H_2O \overset{C.A.}{\rightleftharpoons} H_2CO_3$

↓

$H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$

★ CHLORIDE SHIFT

→ As H_2CO_3 dissociates in H^+ & HCO_3^-, HCO_3^- conc in red cells ↑ses.

↓

HCO_3^- leaves the red cell & exchange of Cl^- from plasma to maintain electrical neutrality

↓

Occurs by $Cl^- - HCO_3^-$ exchanger (⊕nt in red cell membrane)

↓

This exchanger is k/n as Anion - Exchanger 1 (AE1)

↓

* This Cl^- movement in exchange for HCO_3^- is c/d Chloride shift

→ H^+ form during rxn cannot diffuse out b/c of low permeability of mem. to H^+

↓

Most of H^+ is buffered by Hb

↓

$HbO_2 + H^+ \rightleftharpoons HHb + O_2$

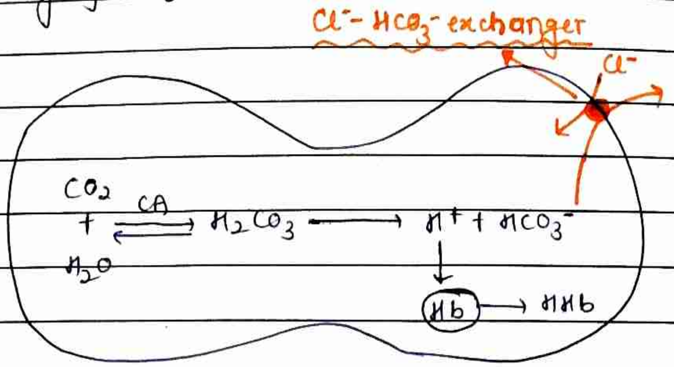
↓

H^+ binds to Hb, ↓se O_2 binding of Hb & shifts the curve to right.

OPPO A53
2022/07/15 23:29

→ This facilitates release of O_2 from Hb in tissue

→ Reverse process occurs in pulmonary capillaries (Reverse chloride shift), where oxygenation of Hb favours un-loading of CO_2.


$Cl^- - HCO_3^-$ exchanger
Cl^-
$CO_2 + H_2O \xrightleftharpoons{CA} H_2CO_3 \longrightarrow H^+ + HCO_3^-$
Hb
HHb

Mechanism of Chloride shift

3. As Carbamino Compounds

→ CO_2 in red cells also reacts with free NH_2 (amine) of Hb to forms Carbamino-Hb

$$CO_2 + NH_2 \rightleftharpoons HbNHCOOH$$

→ Deoxygenated Hb binds more CO_2 then oxygenated.

→ Small amount of CO_2 also combines with plasma protein to form Carbamino-protein-Complexes.

HALDANE EFFECT

→ when blood passes through pulmonary capillaries, O_2 diffuses into blood & forms Oxy-Hb.

→ oxygenation of Hb, shifts the CO_2 dissociation curve to right & Hb begins to lose CO_2

OPPO A53
2022/07/15 23:29

→ ∴ In lungs, Loading of O_2 facilitates unloading of CO_2

Significance

1. Release of CO_2 from blood into alveoli of lungs.
2. Uptake of O_2 by blood

OPPO A53
2022/07/15 23:29

Date
Page

⑪ REGULATION OF RESPIRATION

→ Regulation of respiration differs from regulation of other systemic function for having both automatic & voulantry control mechanism.

→ Nrmlly quite breathing occurs b/c of 2. regulatory mechanisms :- 1. Nervous Mechanism
2. Chemical Mechanism

★ NERVOUS MECHANISM

Respiratory Centers

→ Groups of neurons which controls rate, rhythm & force of respiration.

→ These centers are bilaterally situated in reticular formn of brainstem.

→ Classified in 2 types :-

1. Medullary Centers

→ Medulla controls basic rhythm of respiration.

→ Two diff^n grps of neurons that are well defined in medulla are :-

a) Dorsal Respiratory Group of Neurons

→ Diffusely situated in the nucleus of Tractus Solitariu ⊕nt in upper part of medulla

→ The neurons collectively c/d Inspiratory Centers
↓
b/c all neurons are inspiratory neurons & is primarily responsible for Inspiration & for integration of sensory information.

OPPO A53
2022/07 3:29

b) Ventral group of Respiratory Neurons

→ ⊕nt in Nucleus - Ambiguous & Nucleus - Retroambiguous &
Nucleus - Paraambiguous

→ these 2 nuclei are situated in the medulla oblangata antero-lateral to nucleus tractus solitarius

→ Collectively, the neurons were c/d Expiratory Centres earlier
→ VRG contains both Expiratory & Inspiratory neurons
↓
cells in nucleus retro-ambiguous → active during expiration
cells in nucleus para-ambiguous → active during inspiration

→ Parts of VRG :- Has 3 parts
Rostral, Caudal → expiratory neurons are ⊕nt.
Middle → Inspiratory neurons are ⊕nt

→ Function :- • Nrmlly, inactive during quite breathing & becomes active during forced breathing.
• During forced breathing, neurons stimulates both inspiratory & expiratory muscles.

2. Pontine Centers

In pons there are 2 respiratory centers :-

a) Pneumotaxic Center
→ Situated in dorso-lateral part of Reticular formn in upper pons.
→ Formed by neurons of medial parabranchial & [illegible]-branchial

OPPO A53
2022/07/15 23:29

nuclei (also c/d ventral Parabranchial / Kölliker - Fuse nucleus)

Functions :- • Neurons are active in both inspiration & expiration

- 1° function is to control medullary respiratory centers, particularly dorsal gr. of neurons.
- Inhibits the apneustic center so that dorsal gr. neurons are inhibited

↓

- b/c of this Inspiration stops & expiration starts, thus influences switching b/w Inspiration & Expiration

It ↑ses the Respiratory Rate by reducing the duration of inspiration.

b) Apneustic Center

→ Situated in nuclei reticular formn of lower pons (Caudal Pons)

Function :- • ↑ses depth of inspiration by acting directly on dorsal gr. of neurons.

→ Stimulation causes apneusis (abnrml pattern of respiration)

↓

prolonged inspiration followed by short expiration

OPPO A53
2022/07/

Role of Vagus Nerve

- → Vagus Nerve carries afferent fibres from lung & airways
- → Afferent vagal impulses inhibits the medullary inspiratory neurons, so mag. of inspiration ↓ses.
- → Vagus N. & pneumotaxic center keep the activity of apneustic centre in check.

↓

apneustic centre nrmlly activates inspiratory drive, which is inhibited by vagus N. (vagotomy stimulates inspiration)

- → Vagotomy ⇒ stimulates Inspiration
- Vagotomy + lesion of Pneumotaxic Centre ⇒ Apneusis

Control by Higher Centers

- → Many centers influences the activity of medullary respiratory centers, influence from Reticular Activating System (RAS) & limbic system is more prominent.

Integration of Neural Mechanism

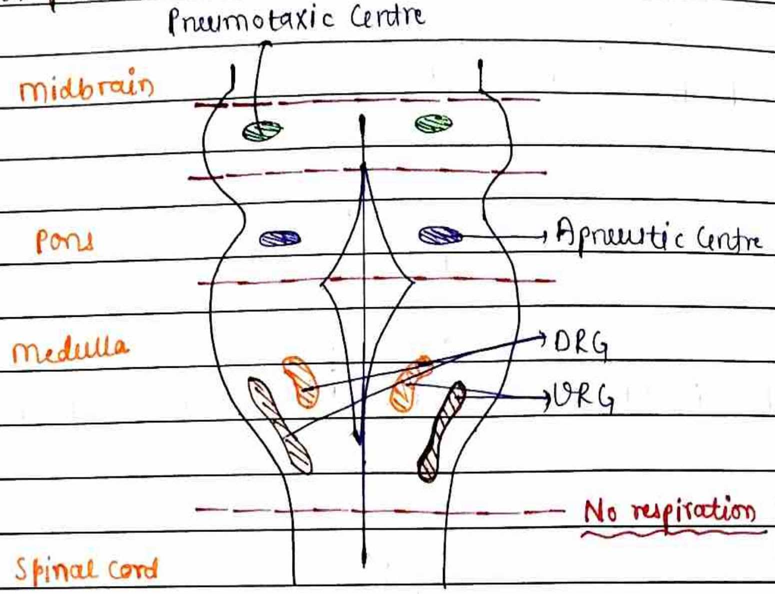
- → Transection of brainstem below medulla completely abolis respiration
- → Above medulla ⇒ basic rhythm of respiration occurs, but respiration is irregular.

↓

this indicates that basic rhythm of respiration is generated in medulla

OPPO A53
2022/07/15 23:29

→ Lesion above pons does not affect respiration, which indicates that controlling centers are located mainly in pons.


Pneumotaxic Centre
Midbrain
Pons
Apneustic Centre
Medulla
DRG
VRG
No respiration
Spinal cord

★ **CHEMICAL CONTROL** (Control by H^+, Pco_2 & Po_2)

→ Breathing activities are directly related to Pco_2, H^+ & indirectly to Po_2.

→ Hypoxia, Hypercapnia & Acidosis stimulate respiration that raise Po_2, lowers Pco_2 & raise P_H.

→ Two sets of receptors that detect these chemical changes are :-

1. Peripheral Chemoreceptors

→ Located in carotid & Aortic bodies.

Mechanism of Action

OPPO A53
2022/07 15 23:29

→ Hypoxia (↓ PO_2) is most potent stimulant for peripheral chemoreceptors.

↓

b/c of presence of O_2- sensitive K^+ channel in glomus cells of peripheral chemoreceptors.

↓sed Ventilation

↓se in PO_2 in blood (main effect)

↑se H^+ in blood (mild effect)

↑se Pco_2 in blood (mild effect)

↓

Stimulation of Peripheral chemoreceptors

↓

Afferent Impulses via Hering's nerve & aortic nerve

↓

Stimulation of dorsal gr. of neurons

↓

Efferent impulses to respiratory muscles

↓

↑sed Ventilation

OPPO A53
2022/07/15 23:29

Date
Page

2. Central Chemoreceptors

→ ⊕nt in brain

→ Situated in deeper part of medulla oblongata, close to DRG, this area is k/n as chemosensitive area & neurons are c/d chemoreceptors.

↓

⊕nt in close contact with Blood & CSF

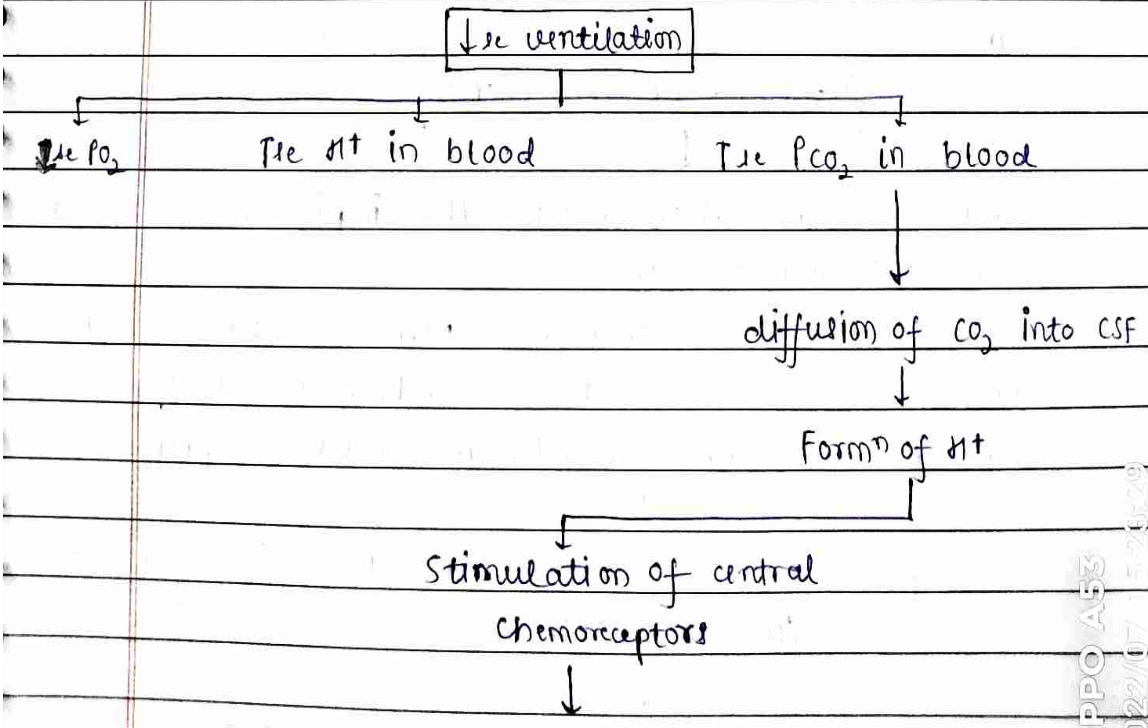
Mechanism of Action

Response to CO_2 & blood pH depends on these receptors.

→ If H^+ conc. ↑ses in blood it cannot stimulate these receptors b/c H^+ from blood cannot cross the blood brain barrier & blood - CSF.

However, CO_2 diffuses readily into CSF & combines with water to form H_2CO_3.

$$CO_2 + H_2O \longrightarrow \underset{\text{(unstable)}}{H_2CO_3} \longrightarrow H^+ + HCO_3^-$$


↓se ventilation
↓se PO_2
↑se H^+ in blood
↑se Pco_2 in blood
diffusion of CO_2 into CSF
Form^n of H^+
Stimulation of central chemoreceptors

Date
Page

Stimulation of dorsal gr. of neurons
↓
Efferent impulses to respiratory muscles
↓
$\boxed{\uparrow\text{sed Ventilation}}$

★ HORMONAL CONTROL

→ Progesterone, $\underbrace{\text{Thyroxine, Cortisol \& Catecholamines}}_{\downarrow}$
↓
↑ses ventilation — influences ventilation

★ NON-CHEMICAL CONTROL

→ Includes reflexes originating from lungs, Airways & chest wall.

★ Impulses from stretch Receptors of lungs

HERING - BREUER REFLEX

↓

→ Protective reflex that restrict the inspiration & prevents overstretching of lungs.

→ Initiated by stimulation of pulmonary stretch receptors which are prsnt on wall of bronchi & bronchioles.

→ Expansion of lung stimulates the stretch receptors
↓
Impulse from receptor reach the DRG via vagal afferent fibre & inhibit them.
↓
So, Inspiration stops & Expiration starts

OPPO A53
2022/07/15 23:30

Date
Page

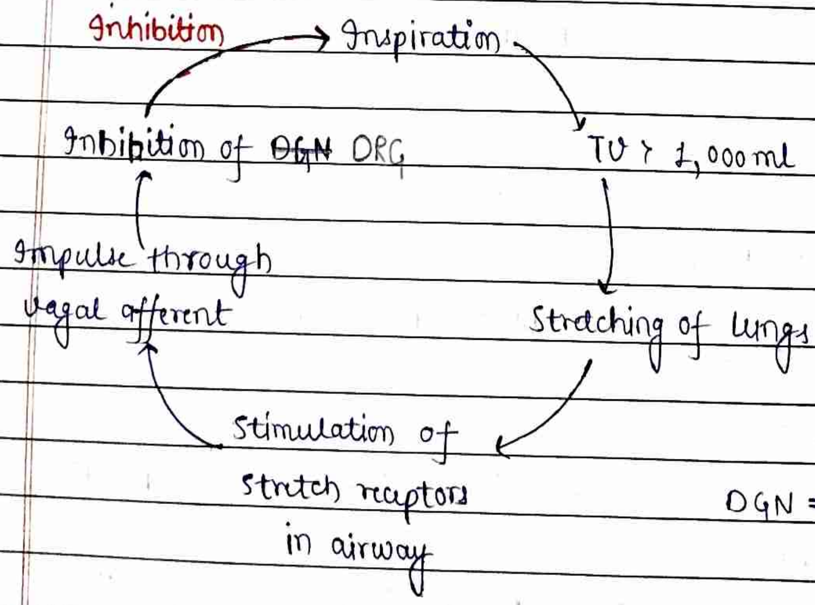
★ Hering Breuer inflation & deflation reflex

→ Above mentioned is Hering Breuer inflation reflex
↓
b/c it restricts the inspiration & limits overstretching of lungs.

→ Reverse of this is Hering Breuer Deflation reflex
↓
takes place during expiration, as stretching of lung is ont, deflation occurs.

★ Significance of Hering - Breuer reflex

1. Protective reflex that protect lung from overinflation.
2. Controls TV during nrml breathing in infants.
3. In adults, does not operate unless TV is much greater then normal inspiration.


Inhibition
Inspiration
TV > 1,000 ml
Stretching of lungs
Stimulation of stretch receptors in airway
Impulse through vagal afferent
Inbibition of ~~OGN~~ ORG

OGN ⇒ Dorsal grp of Neurons

Hering Breuer Inflation Reflex

OPPO A53

⑫ HYPOXIA

→ deficiency of O_2 at tissue level

↓

tissue suffer from hypoxia when supply O_2 is ↓sed or when they fail to utilize the O_2.

Hypoventilation

↓

Hypoxia & Hypercapnia

↓

↑se in rate & force of respiration

↓

Dyspnea

↓ In severe cases

Lethargy

↓

Coma

↓

Death

★ **Types**

1. Hypoxic Hypoxia

→ when PO_2 of arterial blood is reduced

Mechanism

→ PO_2 ↓ses → due to which delivery of O_2 to tissue is reduced.

→ occurs due to low PO_2 in inspired air / disease of respiratory apparatus.

OPPO A53
2022/07/.. 23:30

2. Anemic Hypoxia

→ when Po_2 of blood is nrml but Hb to carry O_2 is not adequate.

→ occurs in condⁿ :-

a) Anaemia

b) CO poisoning

c) Altered Hb (meth-Hb)

Mechanism :-

→ Po_2 of inspired air is nrml

→ diffusion capacity of lung is nrml

→ Po_2 of arterial blood is nrml

But O_2 supply to tissue is reduced b/c Hb is not available

In CO poisoning → affinity of CO for Hb is about 200 times > than that of O_2.

$$CO + Hb \longrightarrow \text{Carboxy-Hb (COHb)}$$

- Release of CO from Hb is very slow. So, O_2 cannot bind with Hb.
- Hb content is nrml but Hb is not available to deliver O_2.
- Hb-dissociation curve shifts to left that ↓es release of O_2 from Hb.

3. Histotoxic Hypoxia

→ Tissue cannot utilize O_2 in spite of nrml O_2 supply.

→ Venous tension of O_2 is high

→ Occurs in tissue poisoning as produced by cyanides.

OPPO A53
2022/07/15 23:30

Date
Page

Mechanism

1. Cyanide poisoning → Cyanide inhibits cytochrome oxidase
↓ treated by Methylene blue/ Nitrites
↓ tissue oxdn is paralysed.

2. Diptheria → diptheria toxin inhibits synthesis of one of cytochrome.

4. Stagnant Hypoxia

→ Occurs due to ↓sed blood flow to the tissue
→ also c/d Hypoperfusion Hypoxia/ Ischemic Hypoxia
↓
as it causes ↓sed perfusion of tissue

Causes :- Heart failure
Shock
Vascular obstruction

Mechanisms :- • O_2 content of blood is nrml
• Occurs due to stagnation of blood in circulation
↓
also c/d Circulatory Hypoxia

• Occurs due to ↓se C.O. / ↓sed flow of blood.

• In severe cases, local acidosis develops

OPPO A53
2022/07/15 23:30

★ Effects of Hypoxia

→ Acute & Severe Hypoxia leads to unconsciousness.

→ Effects of Hypoxia are of 2 types.

1. Immediate Effects

1. Effect on blood

→ Induces secretion of Erythropoietin from kidney

2. Effect on CVS

→ Initially, due to reflex stimulation

↓

- Rate & force of contraction of Heart ↑ses
- C.O. & B.P. ↑ses

later, becomes nrml.

3. Effect on respiration

→ Initially, respiratory rate ↑ses due to chemoreceptor reflex.

4. Effect on digestive System

→ loss of apetite, nausea & vomiting.

5. Effects on kidney

→ alkaline urine is secreted

6. Effect on CNS

→ Symptoms are similar to those of alcoholic intoxication.

→ Individual is depressed with general loss of self-control.

OPPO A53
2022/07/15 23:30

2. Delayed Effects

Person becomes highly irritable, develops symptoms like nausea, depression, vomiting, weakness & fatigue.

★ Treatment

Best is O_2- theraphy
↓
carried out by 2 methods :-

1. By placing patient head in 'tent' containing O_2
2. By allowing patient to breath O_2 either by mask or an intranasal tube.

⑬ DYSPNEA

→ Means difficulty in breathing, also c/d Air Hunger

→ Nrmlly, breathing goes on without consciousness.
↓
- but when breathing enters consciousness & produces discomfort, dyspnea occurs

★ Condn when occurs

→ occurs during severe muscular exercise. (Physiologically)

Pathologically :-

1. Respiratory disorders → • Pneumonia.
    - Pulmonary Edema
    - —— " —— effusion
    - Asthma

OPPO A53
2022/07/.5 23:30

2. Cardiac disorders

common in left ventricular failure & decompensated mitral stenosis.

3. Metabolic disorders

- Diabetes acidosis
- Uremia
- ↑sed H^+ ion conc.

⑭ CYANOSIS

→ Bluish discolouration of skin & mucous membrane.

→ ↓

due to presence of reduced/ deoxy-Hb in more than 5g% in blood.

→ Presence of excess of other Hb-complexes like methemoglobin & Sulfhemoglobin in ~~both~~ blood also causes cyanosis b/c of their dark colour.

Cyanosis is not seen in Severe Anaemia & CO poisoning

↓

(b/c total Hb content is less then 5gm%)

↓

b/c carboxy-Hb prevents reduction of oxy-Hb & colour of COHb is cherry-red.

OPPO A53
2022/07

Date
Page

★ **Types**

1. Peripheral Cyanosis

→ occurs due to slowing of flow of blood through tissue

Causes :- • ↓ed C.O. as occurs in heart failure.
• Local vasoconstriction (Ex:- Cold)
• Venous obstruction
• ↑ed viscosity of blood (Ex:- Polycythemia)

2. Central Cyanosis

→ when reduced - Hb conc is more then 5 gm %.

↓

1. due to mixing of venous & arterial blood
2. due to inadequate oxygenation of arterial blood.

→ Initially, occurs in palate, tongue & inner lip but when amount of reduced-Hb becomes very high it appears in different peripheral sites to.

3. Mixed Cyanosis

→ Both central & peripheral mechanism operates

→ Most common ex. is Chronic-col-pulmonale due to emphysema.

OPPO A53
2022/07/ 5 23:30

MOUNTAIN SICKNESS

→ Condⁿ charaterized by adverse effect of hypoxia at high altitude.

→ Develops in persons going to high altitude for 1st time

* Symptoms

1. Digestive system → loss of apetite, nausea, vomiting b/c of expansion of gases in GI tract.

2. Cardiovascular System → H.R. & force of contraction ↑ses

3. Respiratory System → • Pulmonary blood pr. ↑ses due to ↑sed blood flow
   - Blood flow ↑ses b/c of vasodilation induced by hypoxia.
   - ↑sed Pulmonary B.P. ⟶ causes pulmonary edema
     ↓
     causes Breathlessness

4. Nervous System → Includes headache, depression, dis-orientation, irritability, weakness & fatigue.

* ACCLIMATIZATION

→ adaptations or adjustments by the body in high altitude.

→ Changes during acclimatization

OPPO A53
2022/07/ 5 23:30

1. Changes in Blood

→ RBC count ↑ses, PCV ↑ses & Hb content also ↑ses
↓
due to erythropoietin that is released from JG apparatus of kidney

2. Changes in CVS

→ Overall activity of CVS ↑ses
↓
there is ↑se in rate & ~~velocity~~ force of contraction of heart & C.O.

→ Vascularity in body is ↑sed due to vasodilation induce by hypoxia.

3. Changes in Respiratory System

→ Pulmonary Ventilation ↑ses, this is immediate compensation for hypoxia in high altitude.

→ ↑sed pulmonary blood flow leads to pulmonary Hypertension

→ Due to both of these changes, diffusion capacity of gases ↑ses in alveoli.

4. Changes in ~~Alveoli~~ Tissue

→ cellular oxidative enzymes involved in metabolic rxn & no. of mitochondria ↑ses in persons residing at high altitude.

OPPO A53
2022/07/15 23:30

⑯ **DECOMPRESSION SICKNESS** [Dysbarism, compressed air sickness, Cassion Disease, Bends or diver's palsy]

→ disorder that occurs when a person returns rapidly to nrml surroundings (atm pr.) from the area of high atmospheric pr. like sea.

★ Cause → • High Pr. at deep sea leads to compression of gases in body.

• Among respiratory gases :-

O_2 → utilised by tissue

CO_2 → Expired out

N_2 → Prnt in high conc. i.e., 80% & is an inert gas (neither utilized nor expired)

↓

when compressed by high pr. at deep sea, it escapes from blood vessel & enters into tissue & dissolves in tissue fat & tissue fluid.

★ If the return to surface is fast

→ Escape of N_2 from tissue is fast & bubbles are formed in tissue & blood. This causes damage to tissue

↓

also causes severe pain in tissue, mainly in muscles & joints

→ Underground tunnel workers who uses cassions (pressurised chamber) also develop, c/d Caissons disease

→ Also occurs in person who ascends up rapidly from sea level in an airplane without any precaution.

OPPO A53
2022/07/15 16:30

Date ______
Page ______

★ **Symptoms**

→ Symptoms are mainly due to escape of N_2 from tissue in forms of bubbles.

1. Severe pain in tissue, especially muscles & joints
2. Sensation of numbness
3. Muscles cramps
4. Bubbles in coronary vessels causes → myocardial ischemia
—— " —— Pulmonary —— " —— → Respiratory Compression
5. Occlusion of blood vessels in brain & spinal cord

★ **Prevention**

while returning to surface the ascent should be very slow

↓

Stepwise ascent allows N_2 to come back to blood without forming bubbles

★ **Treatment**

→ Patient should be recompressed immediately in a pressurised cabin, c/d Recompression chamber.

↓

Then brought back to atm pr. by reducing the pressure slowly.

NOTE factor contributing to severity of decompression is not the absolute ↓se but the %. ↓se in pressure.

↓

Rapid ↓se upto 50% is safe but ↓se below 95% is harmful.

OPPO A53
2022/07/15 23:30

Date
Page

⑰ Effects of Exposure to Cold & Heat

1. Exposure to cold

Body temp. is maintained by 2 imp. mechanism
a) Heat production
b) Prevention of Heat loss.

★ Heat Production

→ Produced by following activities

By accelerating metabolic activities

Heat gain center is activated
↓
it activates Sympathetic centers
↓
Cause secretion of Adrenalin & Nor-adrenalin
↓
↑ses production of heat by ↑sing metabolic activities

By shivering

→ Involuntary muscular activity & leads to enormous heat production due to severe muscular activities.

→ 1° motor centre for shivering is situated in post. Hypothalamus near wall of III ventricle.

★ Prevention of Heat loss

Heat gain centre in post. hypothalamus activates
↓
Resulting in cutaneous vasoconstriction & ↓se in blood flow
↓
due to this Heat loss is prevented

OPPO A53

Date ______
Page ______

FROSTBITE

- → freezing of surface of body when exposed to cold.
  ↓
  occurs due to sluggishness of blood flow
- → Exposed areas such as ear lobes, digits of hands & feets are affected.

2. Exposure to Heat

- → Effects of exposure to heat are :-

★ Heat Exaustion

- → Body response to excess loss of water & salt through sweat.
- → Results in loss of consciousness

★ Dehydration Exaustion

- → Dehydration leads to fall in C.O. & B.P.

★ Heat Cramps

- → Severe painful cramps occurs due to reduction in quantity of salt & water.

★ HEAT STROKE – SUNSTROKE

- → Abnml type of Hyperthermia that occurs due to exposure to extreme heat.
- → characterized by ↑se in body temp. above 41°c along with some physical & neurological changes.

OPPO A53
2022/07/15 20:31

→ Hypothalamus loses the power of regulating the body temp.

★ People more susceptible are :-

1. Infants
2. Old people with renal, cardiac, pulmonary disorders
3. People doing physical labour under sun

★ **Features :-**

1. Nausea & Vomiting
2. Headache
3. Abdominal Pain
4. Difficulty in breathing
5. Muscle cramps & convulsion

If immediate treatment not given, results in coma & death.

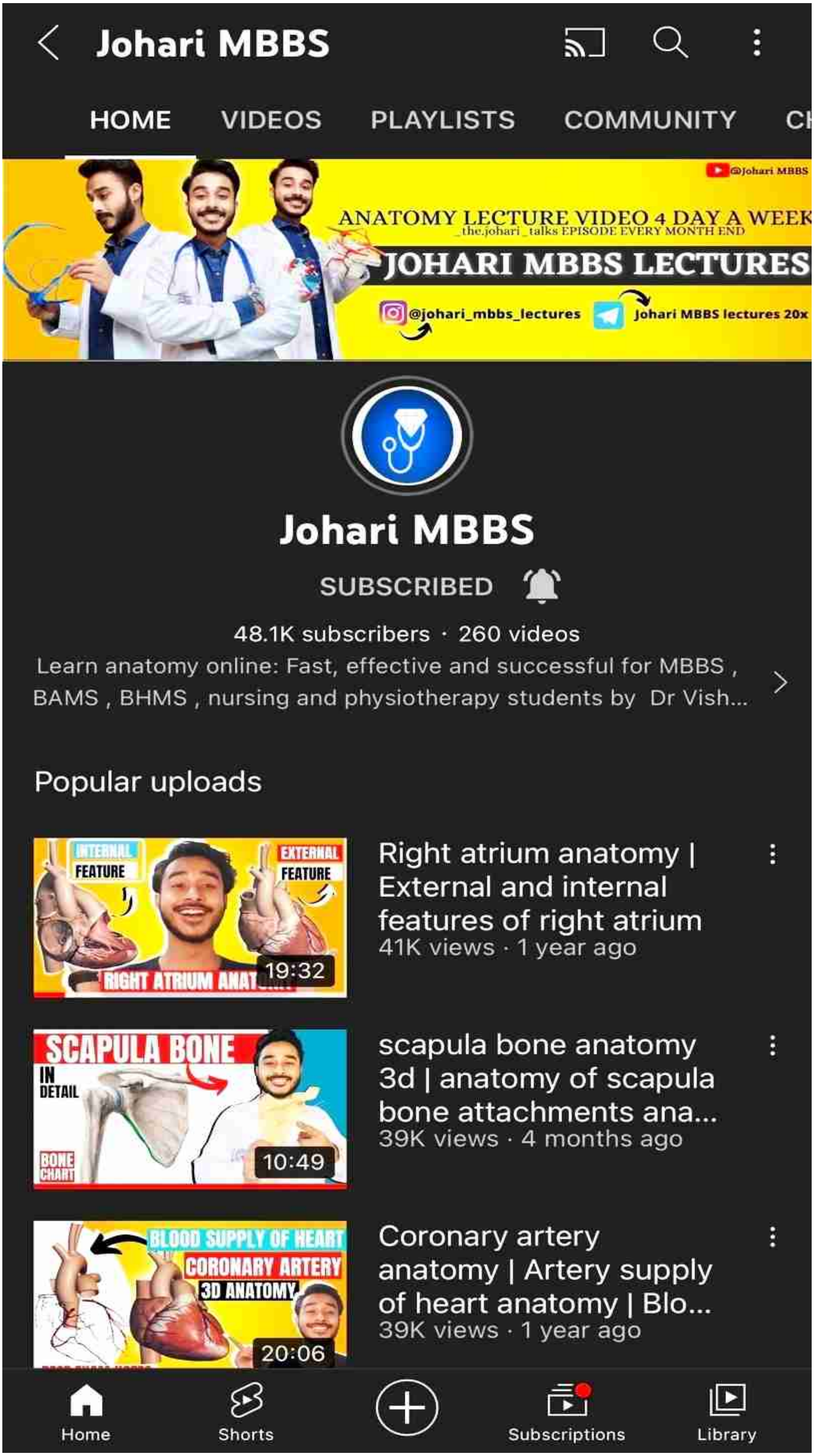
★ **Prevention :-**

1. Avoiding dehydration by taking plenty of fluids
2. Taking frequent breaks during work
3. Wearing ligth clothes

★ **Treatment :-**

→ The person must be immersed in cold water
→ Cooling of head & neck should be done 1st by rubbing ice-cubes.

OPPO A53


Johari MBBS
HOME
VIDEOS
PLAYLISTS
COMMUNITY
CH
@Johari MBBS
ANATOMY LECTURE VIDEO 4 DAY A WEEK
_the.johari_talks EPISODE EVERY MONTH END
JOHARI MBBS LECTURES
@johari_mbbs_lectures
Johari MBBS lectures 20x

Johari MBBS

SUBSCRIBED

48.1K subscribers · 260 videos

Learn anatomy online: Fast, effective and successful for MBBS , BAMS , BHMS , nursing and physiotherapy students by Dr Vish...

Popular uploads

INTERNAL FEATURE
EXTERNAL FEATURE
RIGHT ATRIUM ANAT...
19:32

Right atrium anatomy | External and internal features of right atrium
41K views · 1 year ago

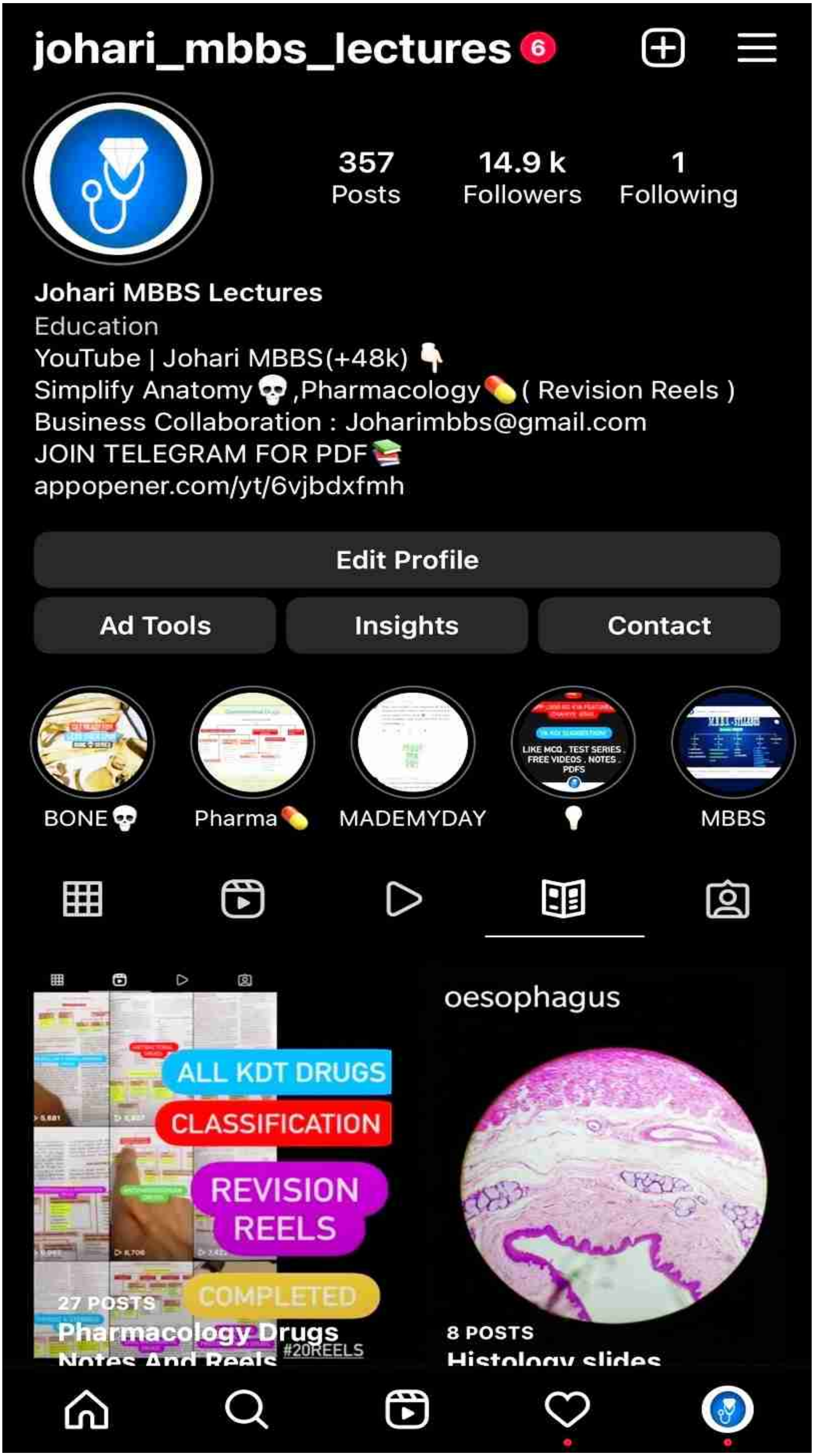
SCAPULA BONE
IN DETAIL
BONE CHART
10:49

scapula bone anatomy 3d | anatomy of scapula bone attachments ana...
39K views · 4 months ago

BLOOD SUPPLY OF HEART
CORONARY ARTERY
3D ANATOMY
20:06

Coronary artery anatomy | Artery supply of heart anatomy | Blo...
39K views · 1 year ago

Home
Shorts
Subscriptions
Library



johari_mbbs_lectures

357 Posts
14.9 k Followers
1 Following

Johari MBBS Lectures
Education
YouTube | Johari MBBS(+48k) 👇
Simplify Anatomy 💀 ,Pharmacology 💊 (Revision Reels)
Business Collaboration : Joharimbbs@gmail.com
JOIN TELEGRAM FOR PDF 📚
appopener.com/yt/6vjbdxfmh

6
Edit Profile
Ad Tools
Insights
Contact
LIKE MCQ , TEST SERIES , FREE VIDEOS , NOTES , PDFS
BONE 💀
Pharma 💊
MADEMYDAY
💡
MBBS
ALL KDT DRUGS
CLASSIFICATION
REVISION REELS
COMPLETED
#20REELS
oesophagus

27 POSTS
Pharmacology Drugs Notes And Reels

8 POSTS
Histology slides